Electroencephalography in encephalopathy and encephalitis

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ABSTRACT

Electroencephalography (EEG) is a useful adjunct to clinical neurological examination, particularly as it may detect subtle or subclinical disturbance of cerebral function and it allows monitoring of cerebral activity over time. Continuous EEG combined with quantitative analysis and machine learning may help identify changes in real time, before the emergence of clinical signs and response to interventions. EEG is rarely pathognomonic in encephalopathy/encephalitis but when interpreted correctly and within the clinical context, certain phenotypes may indicate a specific pathophysiology (eg, lateralised periodic discharges in HSV-1, generalised periodic discharges in sporadic Creutzfeldt-Jakob disease, and extreme delta brushes in anti-n-methyl-D-aspartate receptor autoimmune encephalitis). EEG is included in some specialist guidelines for disease assessment, monitoring and prognostication (ie, hepatic, cancer immunotherapy, viral, prion, autoimmune encephalitis and hypoxic ischaemic encephalopathy). EEG is invaluable for confirming or excluding non-convulsive seizures or status epilepticus, particularly in critically ill patients, and in understanding new concepts such as epileptic encephalopathy and the ictal–interictal continuum.

INTRODUCTION

Electroencephalography (EEG) is not required for the clinical diagnosis of delirium or coma caused by acute encephalopathy (alteration of brain structure or function) or encephalitis (brain inflammation). However, EEG is frequently requested for these overlapping conditions in current practice for the following reasons:

- As an index of, or to monitor, diffuse cerebral function.
- To assess a liability to concurrent symptomatic seizures.
- To distinguish organic from non-organic (functional or psychiatric) presentations.
- To distinguish encephalopathy/encephalitis from non-convulsive status epilepticus (NCSE) or physiological states (such as sedation or sleep), which may coexist.

There is a generally held perception that the EEG changes are rather non-specific in this setting, and therefore, might contribute little to finding the cause. However, the EEG is sensitive to disturbances in cerebral state and function, to the point where EEG changes may precede detection of clinical signs. Furthermore, in certain circumstances, EEG phenotypes may give aetiological insights and prognostic indices.

The distinct advantages of EEG are that it:

- Is non-invasive and relatively painless,
- Is portable, so can be brought to the patient's bedside,
- Is reasonably widely available in clinical practice (in neuroscience centres in the UK at least),
- Is relatively inexpensive (average cost in the UK £218 in adults and £266 in children),
- Can be interpreted and reported in real time.

The disadvantages of EEG are that it:

- Is poorly sensitive for interictal epileptiform discharges (29%–56%) but highly specific (>95%), on a standard (20–30 min) interictal EEG,
- Requires expert interpretation, which may not be readily available
- Has only moderate inter-rater reliability in certain circumstances
- Has somewhat limited 24-hour access (in the UK at least)
- Is prone to artefacts that confound interpretation, or worse can lead to misinterpretation.

In this opinion review, we draw on our clinical experiences and attempt to put current practice into perspective in relation to specialist clinical guidelines, where available; we discuss how we might use EEG in specific circumstances

Table 1 EEG use in encephalopathy as suggested in specialist clinical guidelines

Cause	Guidelines that include EEG	Role of EEG
Hepatic	European Association of the Study of the Liver[5]	Prognostication Exclude NCSE
Uraemic	None	
Toxic	None	Exclude NCSE
Cancer immunotherapy	American Society for Transplantation and Cellular Therapy[9]	Exclude focal seizures and NCSE
Viral	International Encephalitis Consortium[10]	Prognostication
ADEM	None	Differentiation from viral encephalitis
sCJD	MRI-CJD Consortium criteria[15]	Diagnosis and differentiation of subtypes (Heidenhain variant)
Autoimmune Encephalitis	Subtype recommendations: Paediatric autoimmune encephalitis Autoimmune Encephalitis International Working Group[18] Limbic encephalitis—expert consensus[17]	Exclude focal seizure and NCSE
Hashimoto's	None	Exclude NCSE
Hypoxic Ischaemic	European Resuscitation Council and European Society of Intensive Care Medicine[27]	Prognostication Exclude NCSE

ADEM, acute disseminated encephalomyelitis; CJD, Creutzfeldt-Jakob disease; EEG, electroencephalography; NCSE, non-convulsive status epilepticus.

to help provide personalised patient-centred care (see summary table 1).

We will not review every clinical condition but focus on common acute scenarios, with illustrative examples, to help readers to understand general concepts of when an EEG may help or why it may not. We do not discuss causes of chronic encephalopathy that are largely irreversible, such as trauma, mitochondrial and cerebrovascular disease.

There are few contemporary general classification systems for encephalopathy/encephalitis. However, there are emerging concepts and new conditions, which is why we feel this review is timely. Although there are expert papers on EEG in encephalopathy[1 2] the only attempted comprehensive guideline that we are aware of was originally written in Japanese (2016), and pertained to children.[3] This classifies according to pathogen of the antecedent infection or clinicopathological features, and recommends EEG in acute encephalopathy:

> EEG is recommended because it provides information useful for the diagnosis and treatment of acute encephalopathy. (Grade B)
> 1. Both conventional and amplitude-integrated EEG (aEEG) are useful. It is recommended to conduct either, according to availability in each institution. (Grade B)
> 2. Most patients with acute encephalopathy have EEG abnormalities, including generalised, unilateral and localised slowing of background activity. (Grade B)

Typically, the EEG response to acute encephalopathy relates to the degree of cerebral dysfunction, ranging from mild confusion to coma, with electrographically manifesting progressively as:

- Slowing of the normal posterior dominant rhythm—alpha to theta frequency.
- Emergence of background slower frequencies of rhythmic theta and delta activity.
- Loss of organisation (anterior–posterior gradient), sleep architecture and appropriate 'reactivity' of the normal EEG rhythms to external stimulation (eg, posterior dominant rhythm).
- Often depending on the cause, the emergence of distinct graphoelements such as epileptiform sharp waves, generalised or lateralised periodic discharges, triphasic waves, temporal intermittent rhythmic delta activity (TIRDA), extreme delta brushes (see summary table 2).
- Reduction in the amplitude (suppression), eventually becoming discontinuous, burst suppression and ultimately electrocerebral inactivity (ie, isoelectric or 'flat' trace). For definitions of these electrographic terms see the revised glossary of EEG terms.[4]

METABOLIC

Hepatic

The EEG may be normal in the early stages of hepatic encephalopathy. With increasing hepatic encephalopathy the EEG shows slowing of the posterior dominant rhythm, initially intermittent but progressively with more abundant rhythmic theta and delta activity, and deterioration of EEG reactivity and sleep architecture. Classical triphasic waves may develop with worsening encephalopathy in some patients with high serum ammonia, though their presence does not directly correlate with ammonia concentrations. First described by Foley in 1950 as 'blunted spike-waves' and later named 'triphasic waves' by Bickford and Butt in 1955, triphasic waves were initially considered pathognomonic of hepatic encephalopathy but are now known to be a non-specific EEG feature. Triphasic waves are bilateral and widespread, but often seen with a frontal emphasis and a characteristic anterior to posterior

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Table 2 EEG features in certain encephalopathy/encephalitis causes

Cause	Diffuse Slowing	Sharp waves	Periodic discharges	Triphasic waves	Additional features
Hepatic	+/++	–	+/–	+	
Uraemic	+/++	+/–	–	/+	Asymmetry
Toxic	++	–	–	/+	Fast activity due to sedating agents
Viral	++	+/–	+/–	–	Lateralised periodic discharge: HSV-1 Generalised periodic discharge: SSPE, COVID-19
ADEM	++	–	–	–	
Sporadic CJD	+	+/–	+/–	+/–	Suppression
Autoimmune encephalitis	+	+/–	+/–	–	Extreme delta brush: anti-NMDA-R Sharp waves and temporal intermittent rhythmic delta activity: Limbic encephalitis
Hashimoto's encephalopathy	++	+/–	+/–	+/–	Focal slowing
Hypoxic–ischaemic	+/++	+	++	+	Burst suppression, suppression, loss of reactivity

++=abundant, +=present, –=absent.
ADEM, acute disseminated encephalomyelitis; CJD, Creutzfeldt-Jakob disease; EEG, electroencephalography; NMDA-R, n-methyl-D-aspartate receptor.

gradient (figure 1). The European Association of the Study of the Liver guidelines[5] suggests that EEG may help to diagnose minimal hepatic encephalopathy when there are only minor clinical signs or symptoms, and to exclude NCSE. In the later comatose stage of hepatic encephalopathy, the EEG becomes suppressed, usually indicating a poor prognosis.

Uraemia

The EEG features in uraemic encephalopathy are also well described historically and there are studies documenting proportionate changes in serial EEGs of patients with progressive chronic kidney disease, as well as showing electrographic improvements with therapeutic intervention.[6] Non-specific EEG changes are initially similar to those found in hepatic encephalopathy with slowing of the posterior dominant rhythm and progressive generalised or regional slowing, such as frontal intermittent rhythmic delta activity (FIRDA) (figure 2), although in uraemic encephalopathy, sharp waves and seizures occur later more frequently. EEG abnormalities can again precede overt clinical manifestations of uraemic encephalopathy, and the degree of slowing correlates with blood urea/creatinine concentrations and glomerular filtration rate. Sharp waves and asymmetries can develop in the later stages of chronic kidney disease and may indicate a poor prognosis. The EEG may also be a helpful prognostic indicator of response to treatment or, conversely, detection of dialysis disequilibrium syndrome and dialysis encephalopathy. However, contemporary guidelines do not recommend EEG as part of chronic kidney disease management (eg, Kidney Disease: Improving Global Outcomes practice guidelines, 2012).

Toxic

Encephalopathy can develop after exposure to various organic solvents such as toluene, heavy metals such as manganese, and medications such as baclofen, lithium, methotrexate, cyclophosphamide, natalizumab and melarsoprol. There are few data on specific EEG phenotypes, but if clinically significant, there is

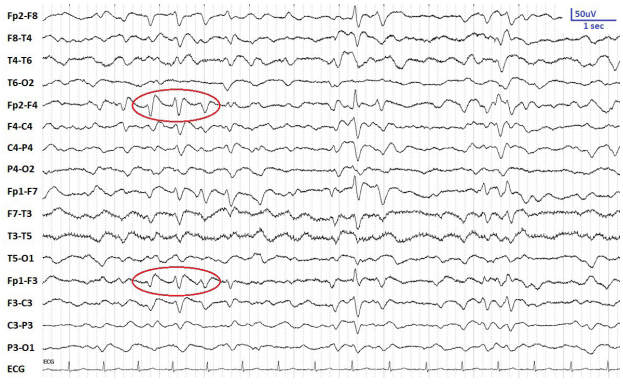

Figure 1 Bipolar longitudinal EEG of a patient with confusion and reduced consciousness due to alcohol-related hepatic encephalopathy: slow background with loss of the posterior dominant rhythm and bifrontal triphasic wave (circled). EEG, electroencephalography.

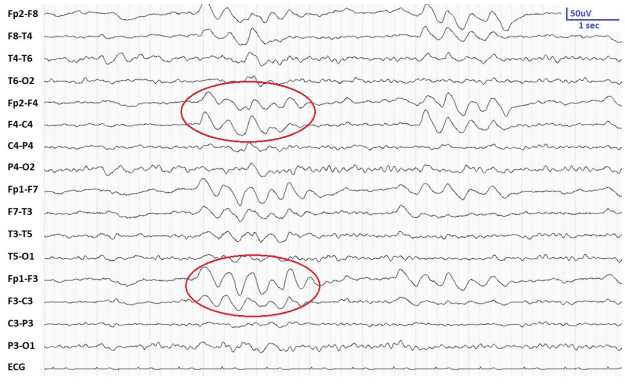

Figure 2 EEG of a conscious patient with uraemic encephalopathy. The EEG shows runs of frontal intermittent rhythmic delta activity (circled) on a mixed frequency background activity with a preserved posterior dominant rhythm. EEG, electroencephalography.

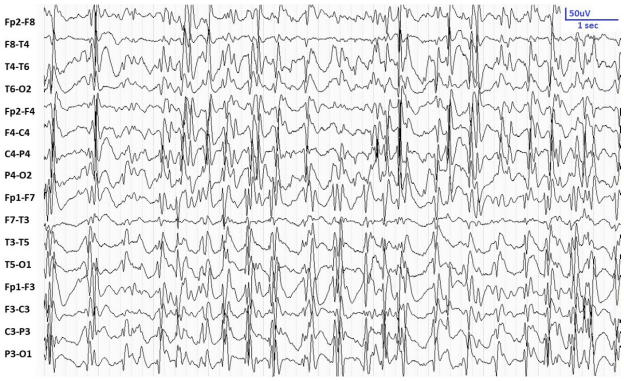

Figure 3 EEG of an unconscious patient now with NCSE, who had been admitted in convulsive status epilepticus. There is near-continuous widespread spikes or spike and slow wave activity at 2–4 Hz.

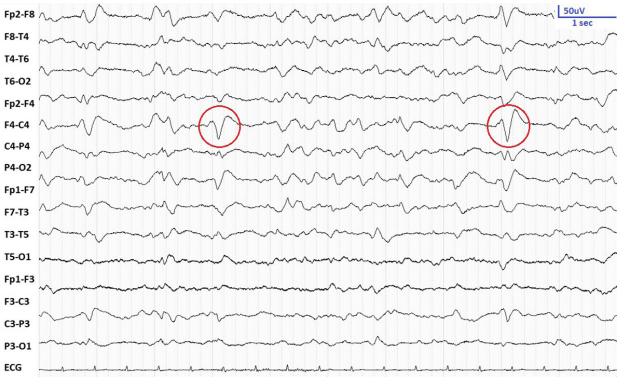

Figure 5 EEG of an unconscious patient with CAR-T-cell-related encephalopathy syndrome following CAR-T therapy for B-cell lymphoma. There is diffuse slowing with triphasic waves (circled). The patient developed seizures and subsequently died. EEG, electroencephalography.

typically diffuse slowing, with loss of the posterior dominant rhythm, reactivity and sleep architecture. In clinical practice, it is common to use EEG to investigate why a patient in a critical care unit is not waking after 'sedation hold', because NCSE is relatively common (figure 3). In those patients with no underlying organic cause, such as NCSE, the typical EEG finding after midazolam or propofol infusion (which itself can cause encephalopathy) is a slow background with superimposed widespread fast activity, suggesting ongoing effects of sedation, and sometimes normal sleep phenomena, indicating a favourable prognosis (figure 4). Although there are no specialist guidelines, a consensus statement by neurologists and neurophysiologists suggested that 'continuous EEG monitoring is an emerging technique to identify secondary brain injuries, seizures and ischaemia in critically ill patients, as well to assess level of consciousness in patients receiving intravenous sedation or pharmacologically induced coma'.[7]

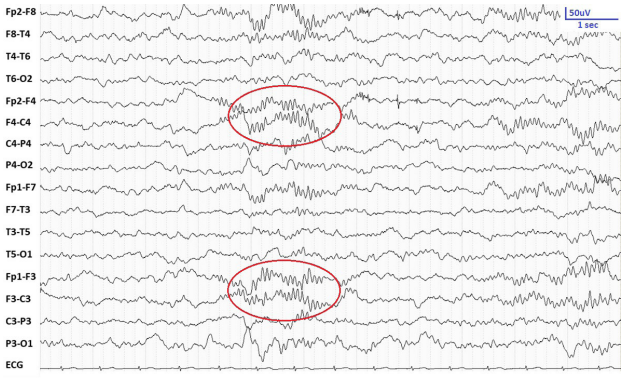

Figure 4 EEG of an unconscious patient on an intensive care unit who was 'slow to wake' after propofol infusion. There are runs of widespread but anterior predominant fast activity (circled), on a slow background. The patient subsequently awoke with no neurological sequelae. EEG, electroencephalography.

CANCER IMMUNOTHERAPY

New cancer immune effector cell therapies offer potential cure in patients with certain refractory haematological malignancies, using genetically modified chimeric antigen receptor T-cells (CAR-T). Immune effector cell-associated neurotoxicity syndrome is a recognised complication and potentially life-threatening with an evolving pathophysiology. Encephalopathy, seizures and raised intracranial pressure can occur, with the EEG typically showing diffuse slowing, occasionally generalised periodic discharges, triphasic waves and sharp waves (figure 5), or electrographic seizures if the condition is severe. The Society for Immunotherapy of Cancer recommends EEG in suspected cases of encephalopathy/encephalitis during treatment with immune effector cell therapies.[8] EEG forms part of the American Society for Transplantation and Cellular Therapy grading for CAR-T-cell-related encephalopathy syndrome with focal seizures or NCSE that resolves with intervention in grade 3, and bilateral convulsive or prolonged NCSE in grade 4,[9] which require critical care and antiseizure medication.

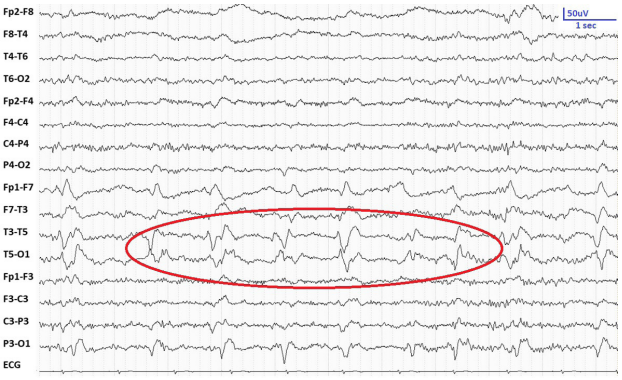

Figure 6 EEG of a patient with HSV-1 encephalitis, showing left temporal lateralised periodic discharges (circled). EEG, electroencephalography.

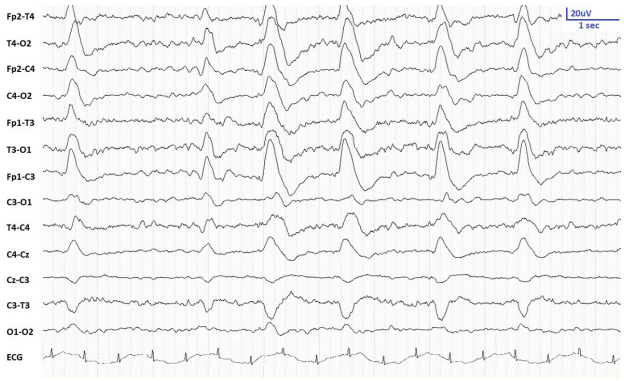

Figure 7 EEG of a child with COVID-19 encephalitis, showing bifrontal maximal generalised periodic discharges. EEG, electroencephalography.

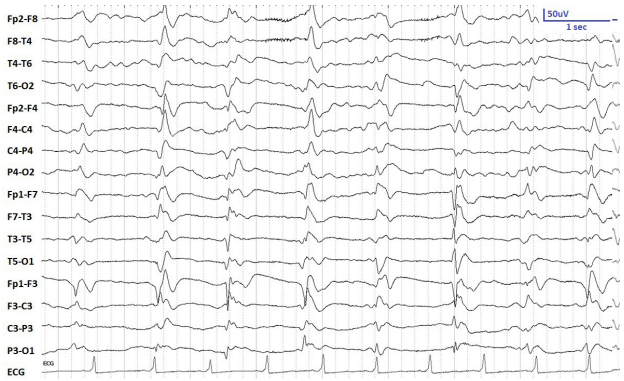

Figure 9 EEG of a patient with sporadic CJD, showing generalised periodic discharges at ~1–1.5 s intervals on a suppressed background. EEG, electroencephalography; CJD, Creutzfeldt-Jakob disease.

INFECTIVE AND PARAINFECTIVE CAUSES

Viral

Viral encephalitis is characterised by brain inflammation due to direct infection of the brain parenchyma, although a pathogen is not always identified or isolated. EEG abnormalities may be non-specific such as diffuse slowing with loss of posterior dominant rhythm, or show distinctive phenotypes, for example, lateralised periodic discharges in herpes simplex virus-1 (figure 6), and generalised periodic discharges in subacute sclerosing panencephalitis. Focal EEG abnormalities should prompt neuroimaging, already an essential part of the assessment of encephalitis, which may, for example, identify additional cerebral lesions in COVID-19 or opportunistic infection in HIV. Lateralised periodic discharges or sharp waves have prognostic significance, indicating an increased risk for developing symptomatic focal onset seizures due to parenchymal involvement. The International Encephalitis Consortium recommends using EEG as one of their minor diagnostic criteria for encephalitis/encephalopathy of presumed infective or autoimmune cause, that is, 'abnormality on EEG that is consistent with encephalitis and not attributable to another cause'.[10]

COVID-19 infection

There are several neurological manifestations now recognised in a considerable proportion of patients hospitalised with SARS-Co-V2 virus. Putative pathophysiological mechanisms include hypoxia, systemic illness, hypercoagulability, endothelial dysfunction, general critical illness, inflammatory response and neurotropism. Encephalopathy is perhaps the most common severe neurological symptom. EEG may be performed due to unexplained altered mental status and typically shows diffuse symmetrical slowing with loss of posterior dominant rhythm. However, its pathophysiological heterogeneity is perhaps expressed in various EEG patterns with focal or regional slowing, occasionally generalised or lateralised periodic discharges (figure 7), as well as sharp waves, which raise the suspicion of additional parenchymal pathology. EEG may be used to prognosticate after

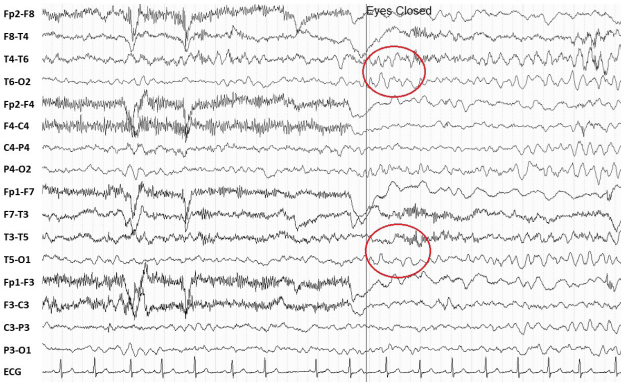

Figure 8 EEG of a child with myelin-oligodendrocyte glycoprotein antibody associated ADEM: mild slowing with a posterior dominant rhythm of 4 Hz on eye closure (circled). ADEM, acute disseminated encephalomyelitis; EEG, electroencephalography.

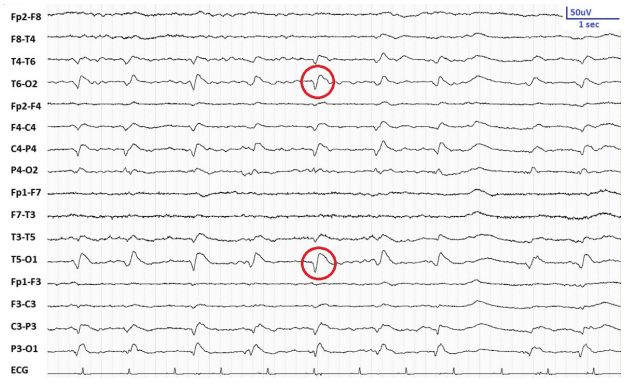

Figure 10 EEG of a patient with sporadic CJD Heidenhain variant, showing bioccipital periodic discharges with triphasic morphology at ~1 s intervals (circled). EEG, electroencephalography; CJD, Creutzfeldt-Jakob disease.

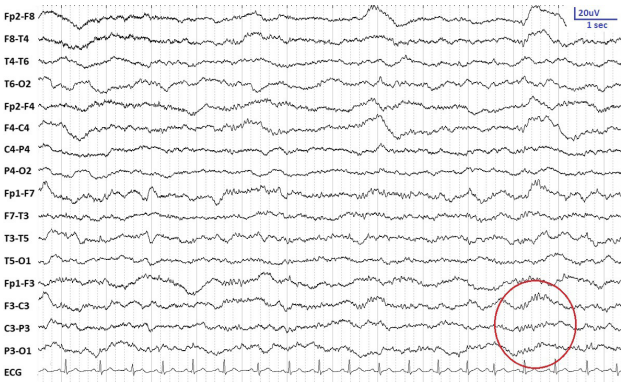

Figure 11 EEG of a young woman with an ovarian teratoma and anti-NMDA-R autoimmune encephalitis: extreme delta brush (circled), comprising delta waves superimposed by fast activity. EEG, electroencephalography; NMDR-R, n-methyl-D-aspartate receptor.

hypoxic ischaemic events and is useful in detecting NCSE in Critical Care. Although clinical seizures are relatively rare in COVID-19 infection, electrographic seizures in the critically ill are an independent predictor of in-hospital mortality.[11] As yet, there are no pertinent specialist guidelines for using EEG in COVID-19.

Sepsis

Septic-associated encephalopathy is a manifestation of extracerebral sepsis ranging from mild delirium to coma; its incidence may exceed that of all intracranial infections put together.[12] Septic-associated encephalopathy has a complex pathophysiology that may involve neuroimmune and neurotransmitter dysfunction, cerebral inflammation and ischaemia, microglial activation, and blood–brain barrier dysfunction (note benzodiazepines should be avoided in this setting—see the Toxic section). EEG findings parallel the clinical severity: in the early stages there may be diffuse slowing, loss of posterior dominant rhythm and emergence of intermittent rhythmic delta activity.

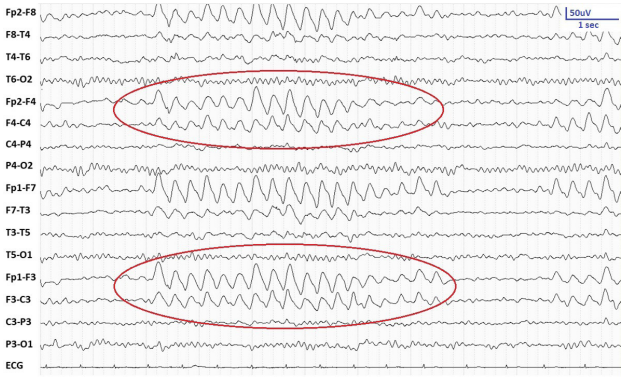

Figure 12 EEG of a conscious patient with hypothyroidism, a history of seizures and antithyroid antibodies, diagnosed as Hashimoto's encephalopathy. The recording shows prolonged runs of peaked frontal intermittent rhythmic delta activity (FIRDA) (circled). EEG, electroencephalography.

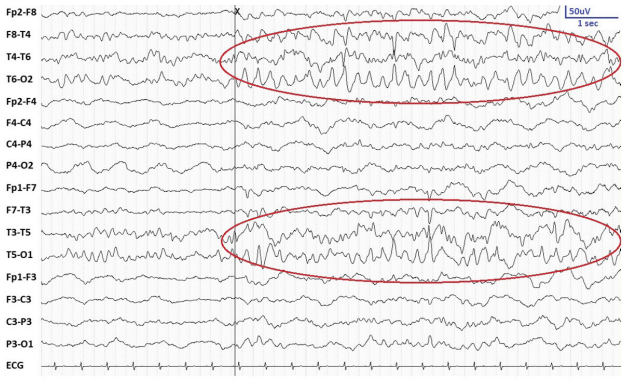

Figure 13 EEG of a child with Dravet syndrome and frequent subclinical electrographic bitemporal ictal activity (circled). EEG, electroencephalography.

With increasing severity other EEG features emerge, including triphasic waves (often associated with multiorgan impairment), sharp waves, lateralised periodic discharges and rarely NCSE. In these cases, serial or continuous EEG monitoring might be used to detect and manage seizures. EEG suppression and loss of reactivity are associated with increased mortality. Septic-associated encephalopathy is associated with an increased in-hospital mortality, and poorer long-term cognitive and functional outcomes.[12 13] There are no specialist guidelines for the role of EEG in septic-associated encephalopathy.

Acute disseminated encephalomyelitis

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated inflammatory demyelinating encephalopathy that affects the brain and spinal cord after a viral or bacterial infection (rarely post-vaccination), usually affecting children and young adults but can occur at any age.[14] The diagnosis is challenging, because of the initially age-dependent heterogeneous multifocal neurological symptoms and signs, and the lack of a specific biomarker. Although MR brain imaging is usually characteristic, an EEG may

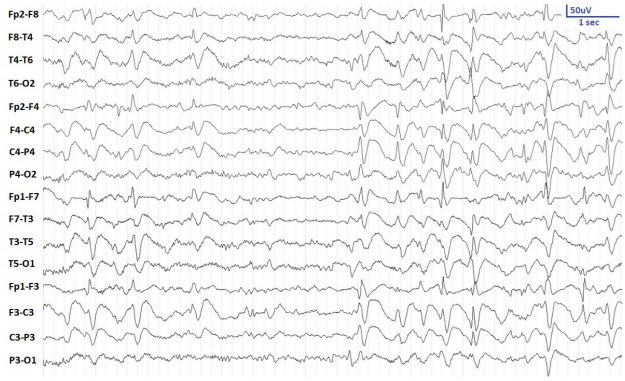

Figure 14 EEG of a patient with Lennox-Gastaut syndrome with near continuous slow 2 Hz spike and wave activity. EEG, electroencephalography.

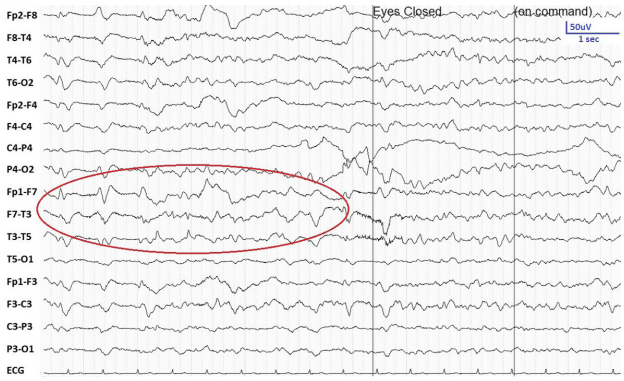

Figure 15 EEG of a responsive patient on a critical care unit after a seizure with ictal-interictal continuum. The EEG shows runs of generalised periodic discharges (triphasic waves and sharp wave morphology) at ~1.5 Hz (circled) that do not evolve but are suppressed by eye closure (ie, reactive). EEG, electroencephalography.

help in establishing organic disease, especially in young children. ADEM is a clinical diagnosis, supported by MRI, but requires exclusion of several differential diagnoses including treatable viral encephalitis, and so an EEG may be requested. The EEG is typically non-specific with diffuse slowing, but focal epileptiform or periodic discharges are rare (figure 8). There are, therefore, no specialist guidelines recommending EEG as part of the diagnostic criteria for ADEM (eg, International Paediatric Multiple Sclerosis Society Group of 2013).

Creutzfeldt-Jakob disease

The characteristic EEG in sporadic Creutzfeldt-Jakob disease (CJD), first described by Abbot in 1959 as a 'fatal illness occurring in the seventh decade progressing steadily to death in 4–8 months', featured sharp waves that may initially be unilateral with a regular time-locked muscle twitch. EEG abnormalities in sporadic CJD typically include progressive changes in background (diffuse slowing, loss of posterior

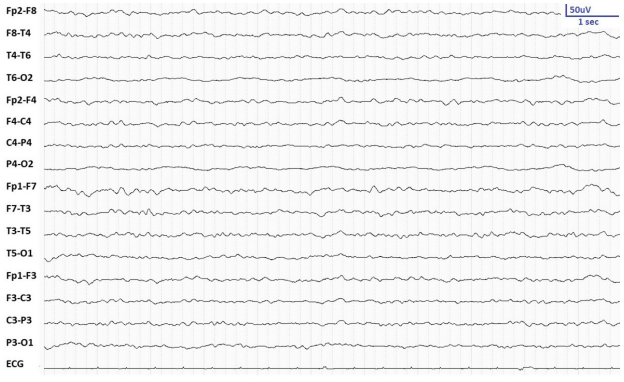

Figure 16 EEG of an unresponsive patient on an intensive care unit after cardiac arrest. The EEG shows continuous mixed frequency background activity. The patient survived without neurological sequelae. EEG, electroencephalography.

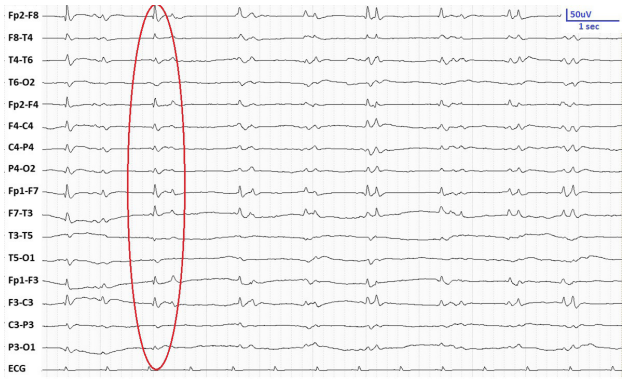

Figure 17 EEG of an unresponsive patient on an intensive care unit after a cardiac arrest. The EEG shows a suppressed background and continuous generalised periodic discharges at ~1 s intervals (circled). The patient died. EEG, electroencephalography.

dominant rhythm and suppression) and emergence of generalised or lateralised periodic discharges (at 0.5–2 s intervals, often associated with myoclonus that may not be time-locked) (figure 9). In the Heidenhain variant, there may be parieto-occipital predominant complexes (figure 10).

Early and reliable diagnosis of this fatal disease is important to counsel patients and their relatives (in the UK referral is made to the National CJD Research and Surveillance Unit (NCJDRSU), University of Edinburgh). There are established diagnostic criteria including clinical features, EEG, MRI and CSF proteins. An update in 2009 found that EEG has the lowest sensitivity of these tests at only 44%, but the highest specificity at 92%.[15] The latest international criteria from 2017, followed by the NCJDRSU, recommend that the diagnosis of probable sporadic CJD is based on typical clinical features with multimodal investigations and corroborating EEG findings of generalised periodic discharges. In the early stages the EEG may be relatively normal or show non-specific slowing, but usually evolves rapidly such that repeat recordings may be warranted at 3–4 weeks intervals. The diagnosis is unlikely if there are no characteristic abnormalities at 12 weeks.[16] However, atypical long duration presentations do occur, and variant CJD does not show classic EEG changes.

AUTOIMMUNE ENCEPHALITIS

Autoimmune encephalitis is associated with high titres of specific IgG antibodies to various neural proteins, including leucine-rich glioma-inactivated protein 1 (LGI1), n-methyl-D-aspartate receptors (anti-NMDA-R), gamma-aminobutyric acid receptors, glutamic acid decarboxylase (GAD), as well as others (eg, Hu, Ma2, aquaporin 4), which may respond to immunotherapy. In clinical practice, heterogeneous presentations with subacute encephalopathy (altered mental status and memory deficits), neurological (including seizures and movement disorders) and

Table 3 TTM-ACNS standardised EEG classification system

Classification	EEG description
Benign	Absence of all malignant features stated below (ie, a continuous EEG of normal amplitude >20 µV±reactivity).
Malignant	Malignant periodic or rhythmic patterns (abundant periodic discharges; abundant rhythmic polyspike-/spike-/sharp-and-wave; unequivocal electrographic seizure). Malignant background (discontinuous background; low-voltage background; reversed anterior-posterior gradient). Unreactive EEG (absence of background reactivity or only stimulus-induced discharges).
Highly malignant	Suppressed background without discharges (<10 µV). Suppressed background with continuous periodic discharges. Burst suppression with or without discharges.

ACNS, American Clinical Neurophysiology Society's; EEG, electroencephalography; TTM, Target Temperature Management.

psychiatric symptoms, require exclusion of potentially reversible disorders (eg, neoplastic, infective, toxic, prion and metabolic processes). EEG is frequently requested as part of the differential diagnostic assessment but may be normal in early presentations of autoimmune encephalitis. In general, typical abnormal EEG patterns with slowing and possible sharp waves are rarely specific, except for an unusual phenotype occasionally occurring in anti-NMDA-R; the extreme delta brush (figure 11). Periodic or rhythmic patterns and seizures appear to confer a poor prognosis. EEG does, however, form part of the expert consensus diagnostic criteria for syndromic limbic encephalitis (associated with Hu, Ma2, LGI2 and GAD), in which there may be temporal sharp waves or temporal intermittent rhythmic delta activity.[17] In children, where anti-NMDA-R encephalitis may be even more common than infective causes, EEG has been recommended to help distinguish autoimmune encephalitis from primary psychiatric disorders and for investigating seizures.[18]

Hashimoto's encephalopathy

Hashimoto's encephalopathy (or steroid-responsive encephalopathy associated with autoimmune thyroiditis) presents with subclinical or mild thyroid disease, usually hypothyroidism and thyroid antibodies (to thyroid peroxidase or thyroglobulin). A seizure disorder, often with prominent myoclonus, occurs in around half to two-thirds of patients, as well as hallucinations and stroke-like episodes. There is no specific EEG phenotype, but frequent abnormalities include diffuse delta activity or FIRDA (figure 12), sharp waves, triphasic waves or generalised periodic discharges, and focal temporal slowing. While confirming seizure activity may help the management, antiseizure medication alone is usually ineffective. Seizures may curtail with clinical improvement after immunotherapy. There are no specialist guidelines recommending EEG for diagnostic confirmation, although in practice EEGs are frequently requested due to seizures and as part of the differential diagnostic workup.[17]

ENCEPHALOPATHY ASSOCIATED WITH EPILEPTIFORM DISCHARGES

Epileptic encephalopathy occurs where epileptic activity (both ictal and interictal) is believed to contribute to progressive disturbances of cognition and behaviour beyond what might be expected from the underlying pathology alone. The International League Against Epilepsy (ILAE) initially recognised eight paediatric syndromes associated with epileptic encephalopathy, but the concept is expanding and may be applicable to epilepsies at all ages and should perhaps be used more widely than just for the severe epilepsies with onset in infancy and childhood. The aim of treatment is first control seizures but also to prevent or even reverse neurological dysfunction, increasingly by hormonal and immune therapies (since traditional antiseizure medication and surgery often have a limited role).[19] This emerging concept is encountered in the following clinical scenarios:

Epileptic encephalopathy

The ILAE includes syndromes (eg, West and Dravet syndrome) and single gene disorders (eg, *CDKL5*, *STXBP1* or *KCNQ2* encephalopathy) which present at an early age with paroxysmal EEG activity that is often aggressive, intractable seizures that are usually polymorphic, and cognitive, behavioural and/or neurological deficits that may be relentless and sometimes fatal. The concept of epileptic encephalopathy assumes that abundant epileptiform activity during brain maturation is the cause of progressive cognitive and neuropsychological deterioration or regression (figures 13 and 14). The possible pathophysiological mechanisms causing neurological compromise include epileptic activity interfering with neurogenesis, synaptogenesis and normal network organisation, as well as triggering neuroinflammation.[20] The EEG changes are often age-dependent with primarily burst-suppression patterns in the neonatal period, hypsarrhythmia in infancy, and slow generalised spike-slow wave discharges in early childhood.[21] The ILAE recommends using EEG to classify epilepsy type and syndrome, supported by the finding of typical interictal EEG phenotypes.[22]

Morris H, *et al*. *Pract Neurol* 2024;**24**:2–10. doi:10.1136/pn-2023-003798

Ictal-interictal continuum

The term 'ictal-interictal continuum', first coined by Pohlmann-Eden in 1996, has largely emerged from continuous EEG monitoring in the critical care domain and refers to the EEG showing generalised or lateralised periodic discharges or rhythmic delta activity (localised or generalised), which are neither ictal nor interictal, but are significantly but variably associated with seizures.[23] Ictal-interictal continuum commonly includes the rhythmic and periodic patterns occurring at a rate of 1–2.5 Hz and lasting at least 10 s (figure 15), but without spatiotemporal evolution or clinical correlates, and so not fulfilling the Salzburg criteria for NCSE.[24] Although the ictal-interictal continuum has uncertain clinical significance, there is concern that it may be associated with cerebral metabolic crisis and an increased risk of seizures that contribute to neuronal injury and poorer outcomes. The emerging electrographic concept of ictal-interictal continuum presents a therapeutic conundrum, and there are currently no evidence-based specialist guidelines for its management.

HYPOXIC–ISCHAEMIC ENCEPHALOPATHY

Hypoxic–ischaemic encephalopathy occurs after cardiac arrest, near drowning or strangulation, with EEG patterns ranging from near normal to suppressed; variably with background slowing, loss of reactivity, epileptiform sharp waves, triphasic waves, generalised or lateralised periodic discharges and burst suppression (figures 16 and 17). One of the first attempts to study the effects of cerebral anoxia systematically on the EEG for neuroprognostic purposes was by Hockaday *et al* in 1965. They produced a five-grade EEG frequency-based classification, which underwent further refinements. More recently the international multicentre target temperature management (TTM) trial provided an opportunity to revisit EEG patterns for neuroprognostication after cardiac arrest, using the American Clinical Neurophysiology Society's (ACNS) standardised critical care EEG terminology: 2012 version.[25] This TTM-ACNS pattern-based system divides EEG phenotypes into: 'highly malignant'—always associated with poor outcome, 'malignant'—nearly always associated with poor outcome and 'benign'—potentially associated with good outcome (table 3).

Furthermore, this standardised TTM-ACNS EEG categorisation also correlates with other validated outcome predictors after hypoxic–ischaemic encephalopathy (ie, clinical signs, chemical biomarkers and somatosensory evoked potentials).[26] It has, therefore, been adopted by the European Resuscitation Council and European Society of Intensive Care Medicine guidelines in the multimodal approach to neuroprognostication after cardiac arrest.[27] What is less clear is the clinical significance of the rhythmic and periodic patterns (generalised or lateralised periodic discharges), and whether treating them with antiseizure medication may ameliorate the potential for further excitotoxic brain injury, although early data suggest not.[28]

List of commonly used EEG abbreviations

- FIRDA—frontal intermittent rhythmic delta activity
- GPD—generalised periodic discharge
- LPD—lateralised periodic discharge
- PDR—posterior dominant rhythm
- SW—sharp wave
- TW—triphasic wave
- TIRDA—temporal intermittent rhythmic delta activity

Key points

- Electroencephalography (EEG) is still useful in the assessment and investigation of encephalopathy and the encephalitides.
- EEG is rarely pathognomonic in these situations but gives an estimate of the degree of cerebral dysfunction and may help neuroprognostication.
- EEG is essential for the diagnosis of non-convulsive status epilepticus.

Further reading

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