Neurophysiology in Neuropsychiatry

CHAPTER 5

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Introduction

Clinical Neurophysiology is a sub-specialty within the field of Neurology which encompasses the diagnostic testing of the biological signals of the nervous system. Primary testing modalities include Electroencephalography (EEG), Electromyography (EMG), Nerve Conduction Studies (NCS), and Evoked Potentials (EP). Diagnostic testing of the peripheral nervous system and muscles is carried out using EMG and NCS. EP studies focus on the functionality of the central nervous system upon application of specific sensory stimuli. EMG, NCS and EP studies show diagnostic changes in the presence of neurological disease and help in the differentiation between organic neurological conditions, from neuropsychiatric conditions such as psychogenic weakness, or visual loss. EEG studies can similarly assist in establishing the difference between a genuine epileptic seizure from a psychogenic nonepileptic seizure. Scalp EEG is a portable, non-invasive test which involves placing surface electrodes on the scalp using soft conductive paste or cream. During the test, the EEG captures the ongoing bio-electrical brainwave signals. Following this, the analysis of the signals can aid in the identification, or exclusion of, contributory physiological or structural pathology in the clinical presentation of neuropsychiatric conditions.

EEG terminology

The understanding and reporting of EEG tests require a clear and precise interpretation of the EEG trace. The ILAE guidelines on the use of EEG terminology aim to ensure non-ambiguous communication of the EEG findings. Reports written for EEG studies interpret the different cerebral waveforms (Table 1). These waveforms can be described in terms of their location corresponding to the region where they derive. The frequency of the waveforms is measured in Hertz (Hz) and are characterised into specific frequency bands named after the Greek alphabet as described in Table 1 and Figure 1.

Table 1 - EEG wave frequencies[2,3]

Wave	Frequency (Hz)
Gamma / High frequency oscillations	> 30
Beta	13-30
Alpha	8-13
Theta	4-8
Delta	0-4

EEG Acquisition

An EEG study is typically set-up and performed by Clinical Scientists or Physiologists specialised in Neurophysiology. Experienced specialists apply surface electrodes to the scalp following the International 10-20 measuring system or Modified Maudsley system. The set-up of an EEG in this way typically takes up to 20 minutes to complete (Figure 2). Often, extra polygraphy electrodes are

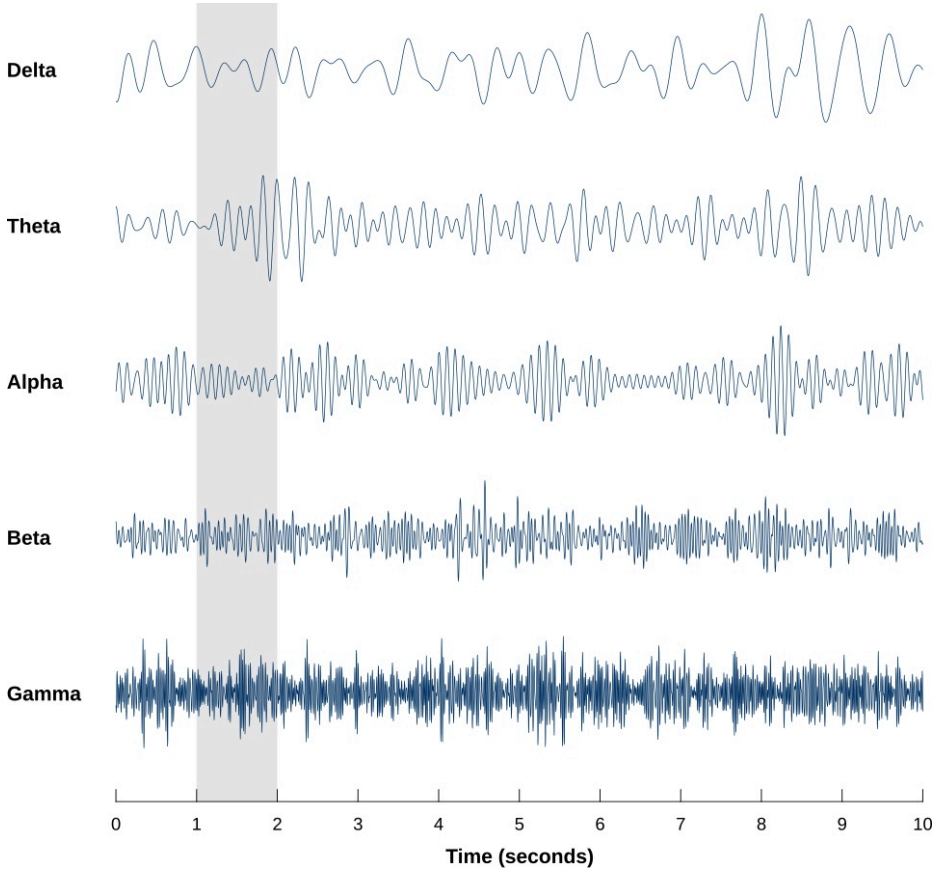


Figure 1 – The differently named frequency bands of neural oscillations, or brainwaves: delta, theta, alpha, beta, and gamma. Attribution to Laurens R. Krol, CC0, via Wikimedia Commons.

applied to record various contributory bio-signals such as electrocardiogram (ECG), surface EMG, electrooculogram (EOG), respiratory, and pulse oximetry. The signals from these electrodes are measured on the EEG recording independently to the cranial signals.

Duration of the EEG study typically ranges from 20 minutes to several day recordings depending on the test type and clinical indication. For example, routine or sleep deprived EEG studies record for 20 minutes and 60 minutes, respectively. Prolonged or home video telemetry (HVT) studies over hours to days, and inpatient telemetry (video EEG) studies may be recorded over several days[3].

Electrodes and montages

Scalp electrodes record the brainwave -electrical signals. The EEG software presents the electrical potentials of each specific electrode channel relative to its position on the scalp. This collection of signals is collated directly onto the computer screen via a montage. A montage is a topographic display of all the recording EEG channels.

The first collection of signals onto the EEG typically are recorded onto a Common Reference Montage; all electrodes are present and each electrode channel appears independently to one another. Montages can be built to reflect the various spatial requirements of the EEG recording. The most used EEG montages are average reference and bipolar derivations. Average referential montages have all electrodes referred to one unifying reference electrode. The resultant average activity is produced because of an active electrode site, and a neutral site electrode calculates the absolute voltage by measuring the waveform amplitude over the area whereby maximal electro-positivity or negativity is present. This montage is particularly beneficial for reviewing generalised electrographic activity[3,4]. Bipolar montages are built in various formats to best depict a range of cortical

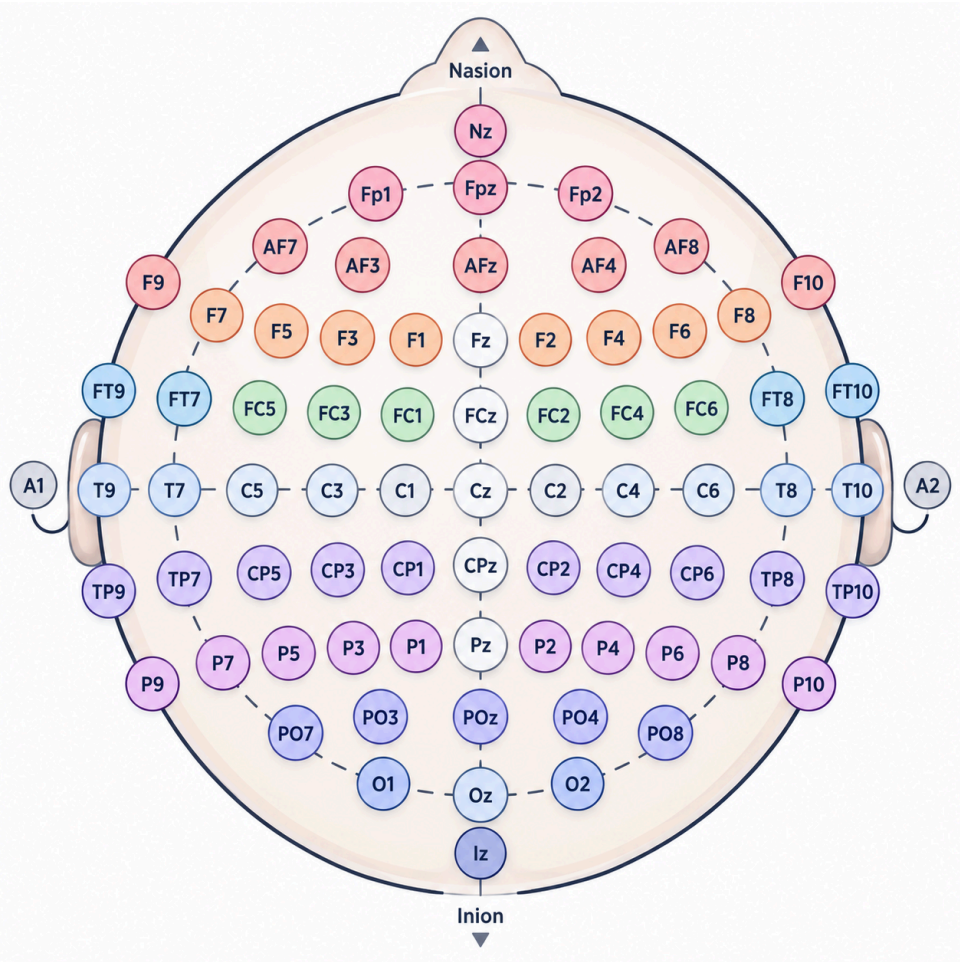


Figure 2 – International 10-20 system placement of EEG electrodes. Re-used from Wikimedia commons under the Creative Commons CC0 1.0 Universal Public Domain Dedication. Credit to Brylie Christopher Oxley.

activity in different directions. Bipolar montages record the potential difference between pairs of active electrodes and can indicate sites of maximum negativity (upwards deflection) through the phase reversal convention. A longitudinal montage runs in a sagittal

orientation (double banana), circumferential and transverse in a coronal orientation. Bipolar montages are particularly useful in localising areas of focal discharges[3,4].

International EEG standards require at least three montages to be recorded during any EEG study; typically include referential, average reference, transverse or longitudinal bipolar montages. EEG recordings are usually performed using the following settings; sensitivity 7uV/mm, and time-base 30mm/sec.

Filters

Signal acquisition and interpretation require filters to control the input of the signal data collected. EEG filters remove unnecessary potentials that mar the recording. These include low frequency filter (LFF), high frequency filter (HFF) and notch filter settings. Typical EEG filter settings are LFF 0.5Hz, HFF 70Hz and notch filters can be used to remove potentials around the 50Hz/60Hz value of the mains electricity in any given geographical location. A LFF removes slower frequencies below the value applied, for example slow waves caused by sweat, patient movement, or poor skin conductance. A HFF removes faster frequencies above the value applied and may be applied to reduce muscle and other artefacts. A notch filter can be applied to reduce mains electrical interference. This value is 50Hz in the United Kingdom. This activity can be remedied through using a ground electrode.

Electroencephalographic artefacts

An artefact is activity which is not solely generated from the cerebral potentials. Artefacts may arise during an EEG study due to physiological or extra-physiological influences. Physiological artefacts occur from the body itself including muscle, EOG movement, sweat, and ECG interference. Extra-physiological artefacts tend to arise from external influences from the body such as mains electrical interference, intravenous lines, in situ devices such as pacemakers or ICD[3–5].

EEG in wakefulness and sleep

One of the first principles to interpret the EEG study is to assess the background rhythm and whether it is appropriate to the age and clinical state of the patient, at the time of the recording. The posterior rhythm is analysed first. In an awake adult, a posterior dominant alpha rhythm is typically seen between 8-12Hz over the bilateral occipital regions (Figure 3). This is best seen during periods of wakeful eye closure. This activity is deemed to be reactive when it attenuates upon eye opening. This can be considered as one of the fundamental hallmarks of a normal EEG in its interpretation[3]. When a person is concentrating or appears to be agitated there may be attenuation of this rhythm during wakeful eye closure. However, if the posterior dominant rhythm is slower or asymmetrical by greater than 50% of the amplitude of the contralateral side, this raises the question of an underlying pathology or underdevelopment of the brain[3].

A short period of sleep may be recorded if the patient is having study lasting longer than 20 minutes. Sleep tends to be categorised into stages as highlighted in Table 2. Stages 1-4 tend to be categorised as non-REM sleep. During REM sleep, the brain appears more active on an electroencephalogram (EEG) compared to alertness. Interestingly, during this sleep phase almost all

muscles of the body are paralysed (REM atonia). The exceptions are respiratory muscles and extraocular muscles. Sympathetic activity predominates during this phase of sleep, which in turn results in an increased respiratory and heart rate. Additionally, during the REM phase, the human brain produces vivid imagery which we know as dreams. NREM sleep is characterised by slow, low-frequency EEG patterns. This phase of sleep is additionally divided into three stages according to the increasing synchronisation of neural activity and lower frequency of generated waves. In contrast to REM sleep, there is usually little or no rapid eye movement and muscles are not paralysed[3]. Additionally, parasympathetic activity prevails, resulting in lowered heart rate, respiration rate and

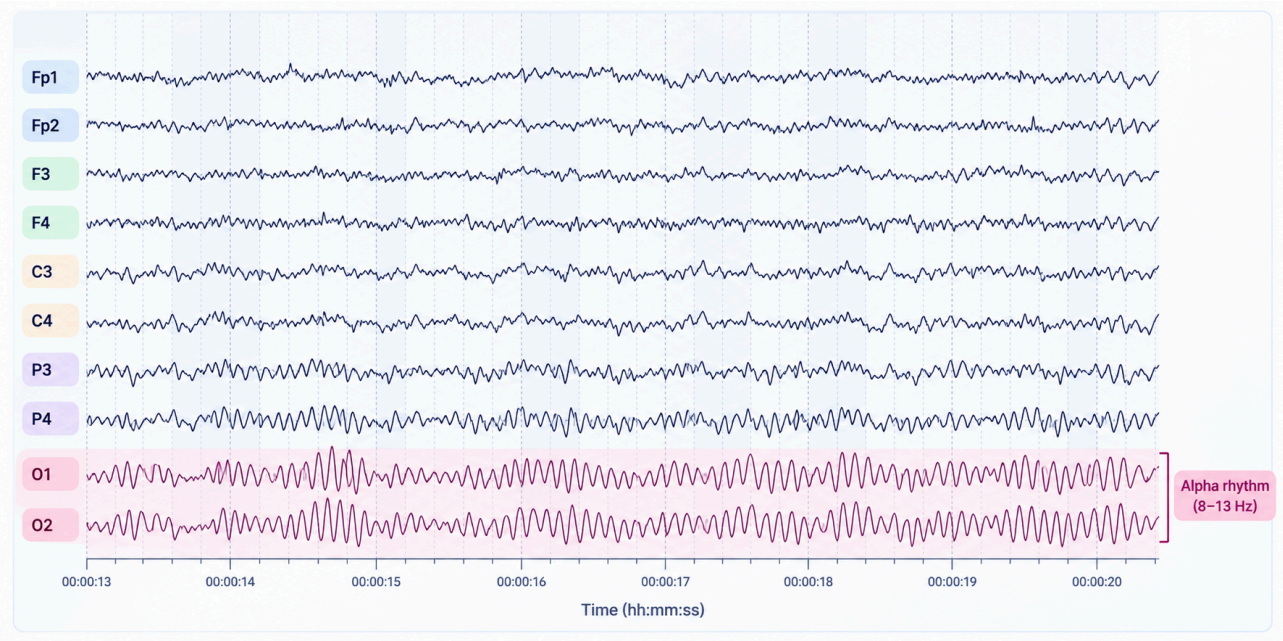


Figure 3 - The sample of EEG with prominent resting state activity during closed eye wakefulness - alpha-rhythm in the occipital regions (bottom two lines O1 and O2). Attribution to Andrii Cherninskyi, CC BY-SA 4.0, via Wikimedia Commons.

renal function, and increased digestion. Natural sleep compared to medicated sleep compared to sleep deprivation. Sleep is known to activate epilepsy[3,4]. In the neurophysiology laboratory for this reason, we often try to record sleep. There are several ways in which sleep can be recorded. Either a patient can undergo a medicated sleep test where they will typically be advised to take Melatonin prior to the test in order to induce sleep, or a patient may be asked to sleep deprive prior to a test. Typically, in the UK, the patient is asked to go to bed two hours later than their usual and wake two hours earlier, thus depriving them of four hours of sleep. More often now in the UK, the preferential way to record a patient's sleep is in the comfort of their own home using home video EEG telemetry. This has many benefits including obtaining natural sleep for the patient in a less disrupted environment than the hospital, removing the need for medicated sleep or sleep deprivation. There are safety benefits to this approach, removing the reduced seizure threshold that sleep deprivation precipitates for example.

Table 2: Sleep stages with corresponding EEG correlate and resultant biological activity[3,4,6]

Stage Name	EEG Frequency	Electromyography	Eye Movements
W Wakefulness	Alpha	++	++
1 Drowsiness	Alpha to theta	++	+ Lateral, slow
2 Light sleep	Theta to delta (<20% delta waves)	-	+
3 / 4 Deep sleep	Delta (level 3 - 20% to 50% delta waves, level 4 - >50% delta waves)	-	+
REM	Alpha / theta	-	++ Lateral, fast

High frequency oscillations (HFOs) are observed during EEG recordings in the frequency range of 80-500 Hz; classified into ripples (80-200 Hz) and fast ripples (200-500 Hz). These ripples and fast ripples have been characterised as a new biomarker for epileptogenesis and ictogenesis. These potentials are particularly challenging to record on scalp EEG as other high frequency activity can interfere with true potential recordings such as frontalis or temporalis muscle activation, or external factors[3,7]

Normal variants in EEG: Upon an EEG, normal variants may arise amongst the background rhythms which are deemed to be normal interictal phenomena. Some examples of benign EEG variants[3,4] include:

- BETS - Benign Epileptiform Transients of Sleep; brief <50 ms and low amplitude >50 μV.
- SREDA - Subclinical Rhythmic EEG Discharges in Adults; abrupt 5-7 Hz, between 40-80 secs duration.
- FOLDS - Female Occipital Low-Amplitude Drowsy; 5-7 Hz “phantom” spike-and-wave bursts.
- WHAMS - Waking High-Amplitude Male Spike; >45 μV.
- Phantom spike waves - short low-amplitude bursts of 5-7 Hz spike-and-slow wave activity in adolescents and young adults.

Interictal epileptiform discharges: Interictal phenomena occur during an EEG whilst an electro-clinical seizure is not happening. When present, these waveforms in (Table 3) increase the risk of an epileptic seizure and may provide support for a diagnosis of epilepsy in combination with the clinical presentation.

Table 3 - Interictal and ictal epileptiform discharges[1,3,4,8,9]

EEG Finding	Appearance on EEG	Clinical Significance
Sharp wave	Transient sharply contoured wave lasting between 70-200 ms	Focal cortical hyperexcitability
Spike wave	Transient spiky waveform lasting between 20-70 ms	Focal cortical hyperexcitability
Spike-and-slow wave Discharge	Sharp/spike followed by a slow wave; often appearing between 150-400 ms	High propensity for seizure activity
Generalised Periodic Discharges (GPDs) (image 3)	Synchronous, widespread across both hemispheres	Negative prognostic indicator in post-cardiac arrest at 12-24 hours
Periodic Lateralised Discharges (PLDs)	Regular repetitive and periodic sharp/spike/complex polyphasic sharp wave and slow waves localised to one hemisphere	Focal irritability or lesion. Acute or subacute focal pathology Transient pattern; usually lasts days to weeks
Bilateral Periodic Discharges (BiPLDs)	Asynchronous, appear across both hemispheres	Multifocal pathology such as Infections, stroke or metastasis
Suppression / Burst Suppression	Attenuated background activity interspersed with bursts of high voltage slow or polyphasic sharp and slow activity.	Post ictal states, refractory status/non-convulsive status epilepticus and post hypoxic or anoxic arrest

EEG in Neuropsychiatry

Seizure Disorders

Temporal Lobe Epilepsy

Temporal Lobe Epilepsy (TLE) comprises approximately 60% of focal epilepsy cases in the general population. TLE can present as focal seizures, with preserved or impaired consciousness, or focal to bilateral tonic-clonic seizures[1]. Underlying structural pathologies such as hippocampal sclerosis or cortical dysplasia may present clinically as temporal lobe seizures. Typically, temporal lobe seizures present with an aura. This may consist of an abdominal rising sensation or psychic phenomena such as a feeling of familiarity, déjà vu or jamais vu. Psychiatric manifestations may include sudden fear, abrupt mood shifts (depression or intense anger), hallucinations, illusions or delusions. Motor manifestations may occur such as dystonic posturing or automatisms of the limbs or extremities depending on the seizure focus (ipsilateral or contralateral). Bilateral, all limb involving, tonic-clonic convulsive seizure may occur secondary to the initial temporal lobe focal seizure. However, typically mesial temporal lobe epilepsy presents with focal impaired awareness seizures,

with postictal confusion and amnesia. EEG correlate typically show focal spike or sharp waves over the anterior temporal lobe and may progress to show generalisation with varying amounts of interhemispheric discharges. Transition from wakefulness into sleep stages commonly activates focal temporal discharges during EEG recordings. Often, ictal or interictal recordings with typical focal epileptic transients are necessary to determine the nature of the clinical signs or symptoms of a temporal lobe seizure as patients may present with non-epileptic seizures upon a background of TLE. An EEG is helpful to differentiate and aid medical management of the presenting symptoms in these cases. When episodic behaviour disturbance or amnesia is being investigated, and epileptiform activity is detected on the EEG, the EEG helps make the diagnosis of epilepsy.

Status epilepticus

The International League Against Epilepsy (ILAE) task force[1] defined the time periods for SE as[1,3,4,9,10]:

- 5 minutes for generalized tonic-clonic seizures
- 10 minutes for focal seizures
- 10 to 15 minutes for absence seizures

Convulsive SE has a presentation of a repeated pattern of generalised or focal motor symptoms, e.g. tonic-clonic or myoclonic. These are commonly associated with loss of awareness or consciousness. Convulsions may be associated with increased temperature in the paediatric population. Non-convulsive SE (NCSE) presents with various semiologies: prolonged altered awareness or consciousness, confusion, delusions, hallucinations, paranoia, tiredness, fugue state, aphasia and abnormal autonomic symptoms. However, there also may be no obvious clinical signs associated.

An EEG is a particularly helpful tool in supporting the management and diagnosis of NCSE. The recorded epileptiform activity in the clinical context of NCSE may be the only indication of seizure activity. The frequency of generalised periodic discharges and any variabilities in their electrographic morphology can be detected and background activities can be assessed in between the epileptic discharges[12]. In some cases, antiepileptic medications can be administered during recording to show response in reducing the frequency, change in morphology and/or amplitudes of the epileptiform activity. Testing the brain's ability to terminate seizure activity in SE can be established and this may aid in the patient management and prognostication.

Case study KS:

History: Patient KS presents with continuous jerking of the right side of her mouth and right arm, present for most of the day and night for the last two months. She describes no loss of consciousness during these episodes. Separately, she has weekly episodes that are convulsive and generalized associated with a loss of consciousness.

Past Medical History: 23-year history of epilepsy, with onset at age five. She was born two weeks prematurely but otherwise had an unremarkable pregnancy and delivery. She has longstanding learning difficulties, having achieved early motor and language milestones. Her psychiatric history includes mood instability with previous self-harm and suicide attempts.

Investigations: Serial video-EEG over more than a decade consistently localised epileptiform activity to the left frontal region, though her continuous facial and arm jerking has never shown a clear surface EEG correlate. The full body convulsions with loss of consciousness were captured on scalp EEG and proven to be non-epileptic attacks. Genetic testing excluded MELAS and POLG mutations were negative. The MRI brain scan showed some left frontal volume loss and encephalomalacic change (Figure 4). A left frontal cortical resection was performed, and biopsy demonstrated chronic encephalitis, supportive of Rasmussen's encephalitis. Single pulse electrical stimulation subsequently identified two independent hyperexcitable foci within the left frontal cortex, and a trial of repetitive transcranial magnetic stimulation produced a temporary reduction in her right-sided jerking.

Treatment: Despite eight concurrent anti-epileptic medications and resective neurosurgery, Patient KS's right-sided symptoms remain relatively unremitting. A trial of intravenous immunoglobulin provided some intermittent symptomatic partial relief however symptoms recurred between infusions, and this was not sustainable. The patient now has neuromodulation was vagal nerve stimulation which has reduced the unilateral jerk frequency and severity by 30%. This case illustrates the difficulty of confirming Rasmussen's encephalitis when biopsy findings are supportive but not conclusive alone, and the importance of distinguishing epileptic from non-epileptic events when both coexist in the same patient.

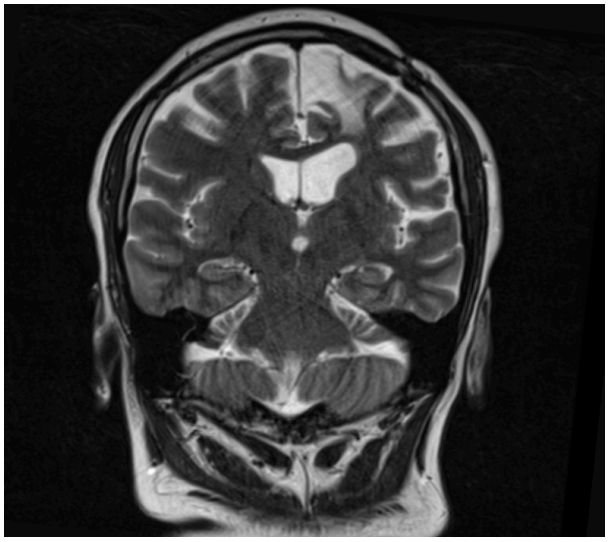


Figure 4: Case study KS: Left frontal volume loss and encephalomalacic change, Disclaimer: All images relating to the case study have approved consent for use by the patient and all information is anonymized.

Epilepsy partialis continua (EPC)

EPC is defined as partial status epilepticus with simple motor manifestations continuing for more than one hour duration with clonic activity restricted to one body part and occurs in regular intervals from rest. The clonic activity may involve any muscle group and is more common in the upper limb. The frequency of the clonic activity varies between 0.1-6Hz. The movement remains in a singular area of the body where the electrophysiological activity originates from. Occasionally, a Jacksonian spread of the seizure occurs leading to a focal to generalised seizure. This activity can continue for hours and up to several weeks. The patient's awareness is retained throughout. Post ictal weakness is present upon seizure cessation[4]. The EEG shows lateralised and generalised but asymmetrical background slowing. The electrographic activity originally commences due to hyperexcitability of the cortex, however, sub-cortical mechanisms have been hypothesised. EPC may be

the clinical presentation of a pre-existing cortical lesion or progressive disease such as Rasmussen's Encephalopathy. The motor activity may be modified by somatosensory stimulation.

Psychogenic non-epileptic seizures (PNES)

PNES, or functional non-epileptic attack disorder (NEAD), present with events which appear to mimic or show similar clinical attributes to an epileptic seizure but does not have associated ictal EEG correlate. However, between 5-20% of patients diagnosed with PNES also have a diagnosis of epilepsy, with both epilepsy subtypes occurring together[4]. PNES is a neuropsychiatric disorder classified as a somatic symptom disorder in the DSM-5[13]. Certain presenting features may indicate PNES such as lack of control despite treatment with anti-epileptic medications, triggers associated with emotion, pain, stress, and sometimes, external stimuli such as lights or sounds (although provocation by flashing lights and some sounds can also occur with epilepsy). There is no overt electrographic correlate of spike wave activity associated with clinical symptoms during an EEG recording and often the posterior dominant alpha rhythm remains sustained and reactive throughout the episode, even when the patient is clinically unresponsive and apparently in 'altered sensorium'. Another feature suggestive of PNES on the EEG is the absence of postictal slowing after the event, or even alpha activity immediately appearing after generalised body jerking. The video recording of the PNES may show asynchronous limb jerking, variability of jerking from one part of the body to the other, dramatic whole body jerking including body arching not typical of tonic-clonic seizure, and prolonged episodes with variable jerking with repeated stop and start. PNES is a feature of a clinical dissociative state and does not arise from electrographic cortical discharges. Prolonged EEG recordings (ambulatory home video telemetry or in-patient video telemetry) are beneficial in the diagnosis of those presenting with suspected PNES by increasing the likelihood of capturing an event. Episodes captured on video EEG, and those confirmed by an eyewitness familiar with the patient and their symptoms, is paramount in differentiating the diagnosis from an organic cause of seizures and substantially benefits the patient as they receive appropriate management of their events. Long term quality of life outcomes for patient's diagnosed with PNES are generally poor and many continue to suffer from functional seizures[3,4,8].

Neurodegenerative conditions

Dementia and Alzheimer's Disease (AD)

Although EEG is not a diagnostic tool in AD, it is sometimes used to determine functionality. When clear changes (see below) are present, EEG can be useful in differentiating AD from other organic or pseudo dementias (dementia symptoms secondary to depression or psychosis)[14]. However, there may be no EEG changes in those presenting with AD and correlation with neuroimaging and pathology is vital.

There have been three EEG observations found to correlate to AD:

1. Diffuse slowing of the EEG background[15]
2. Reduced complexity of the EEG signals with appearance of focal abnormalities (e.g. sharp waves over temporal and frontal areas, with occasional bilateral appearance)

3. Reduction and disappearance of the posterior dominant alpha rhythm

These findings may be due to a decline in functional and cortical connections.

Increasingly, EEG is being used as a biomarker, using signal processing to detect AD and other dementias in the preliminary stages with some indication to severity. Using EEG results of the P300 waveform as a time-sensitive biomarker has been described to correlate with early detection and diagnosis to support current treatment and management of the dementias in the early stages of the structural changes, as described above[16].

Patient state is important to record during the EEG as patients with AD may have a diffusely slow wave background in wakefulness with or without an unreactive posterior dominant rhythm in the alert state. Silent seizures over the hippocampal regions have been described in literature which raises the possibility that the hippocampus is abnormal but which scalp electrodes may be limited in identifying and localising [17].

Encephalopathies

Metabolic encephalopathy

Metabolic encephalopathy is the generalised dysfunction of cerebral function associated with changes in the brain's homeostatic environment. This is due to metabolic, electrolyte or toxic influences which may be reversible if cause is found and managed prior to parenchymal apoptosis. Clinically, the patient will present with an alternation in their conscious level from mild confusion to a comatose state. EEG findings are non-specific, and initially appear to show slowing of the background alpha rhythm to theta range. This activity may further develop into monomorphic delta or frontal intermittent rhythmic delta activity (FIRDA) until there is loss of generalised waveform amplitudes and reactivity to stimuli. Generalised periodic discharges may develop and transform into burst suppression activity.

Hepatic encephalopathy

A serious complication of liver disease (compensated and decompensated) which is displayed as a wide range of neuropsychological clinical findings ranging from minimal signs of encephalopathy to hepatic coma. Hepatic encephalopathy is associated with a decline of mental functioning with apathy, euphoria, irritability and fragmented intellectual ability. In hepatic encephalopathy secondary to liver disease, the EEG may highlight marked electrographic slowing or show triphasic waveforms. The amount of slowing noted on an EEG often mirrors ammonia levels in the blood. In early stages of the enhanced slowing, the alpha rhythm may be preserved and can show fluctuations in the frequency from normal 9-10Hz to alpha normal variants of 5-7Hz or 6-8Hz[19]. Triphasic waveforms are broadened sharpened slow waves with three phases- an initial sharp positive component, a broad negative second component and an even broader third positive component. These waveforms are believed to be hallmarks of hepatic encephalopathy, but not pathognomonic. Triphasic waves can be seen in patients with reducing levels of consciousness but also in patients who are awake.

Autoimmune encephalopathy

Acute encephalitis is defined as inflammation of the brain parenchyma with acute or subacute onset of altered level of consciousness, lethargy, personality change, short-term memory deficits or psychiatric symptoms[20]. This most commonly occurs in young females. Over the last 25 years, advancements in medical research have identified an array of autoimmune encephalitides which previously were considered as cryptogenic neurological disorders. Presentations include psychosis, catatonia, abnormal movements, seizures, memory and cognitive impairment, autonomic disturbances and spinal cord dysfunction. Seizures occur frequently with paraneoplastic limbic encephalitis and may develop into refractory status epilepticus with poor response to anti-epileptic treatments. EEG study is useful to exclude subclinical or NCSE as a primary cause of the encephalopathy presentation, Diffuse slowing or epileptiform abnormalities in the temporal lobes are the commonest findings on EEG.

Anti- NMDAR encephalitis

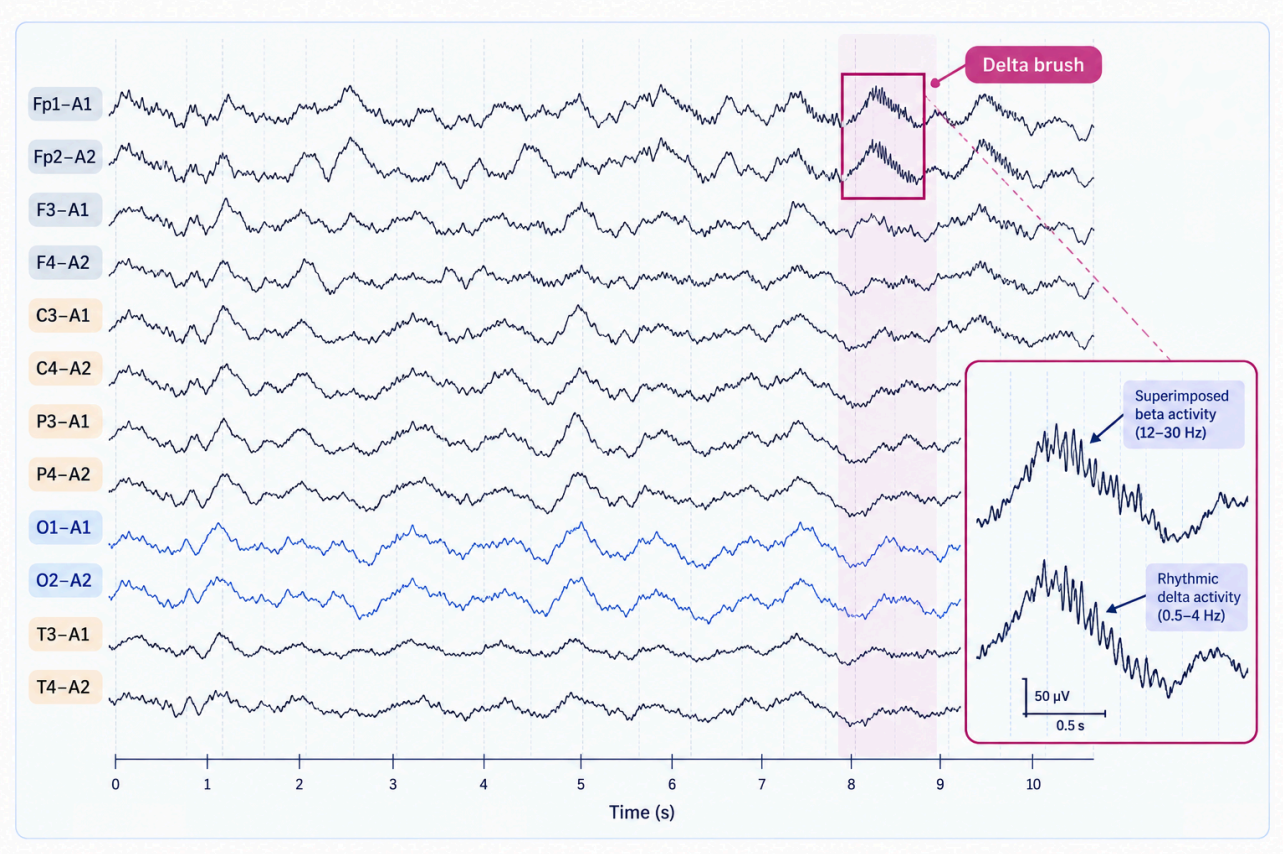


Figure 5 - Extreme delta brush consisting of rhythmic beta activity upon rhythmic delta activity—a waveform specific to patients with severe anti-NMDAr encephalitis. Attribution to Tomotaka Mizoguchi, Makoto Hara, Satoshi Hirose, and Hideto Nakajima, CC BY 4.0 via Wikimedia Commons.

Anti–N-methyl-d-aspartate receptor (NMDAR) encephalitis is an autoimmune encephalitis which initially presents as agitation followed by catatonia and affects primarily young women (75%) and to a lesser extent children and adolescents (25%). Anti-NMDAR encephalitis symptoms include: headache, confusion, memory deficits with amnestic syndrome and encephalopathy, psychosis including delusions, paranoia, visual or auditory hallucinations, dyskinesias such as “piano-playing”

and orofacial involvement, autonomic instability with central hypoventilation, facio-brachial seizures and coma[13]. EEG patterns seen in this autoimmune encephalopathy can include focal or hemispheric slowing and often diffuse background slowing. An extreme “delta brush” (Figure 5) type pattern has been observed in ~30% of patients with anti-NMDAR encephalitis[22]. This pattern can be continuous or become rhythmic and is often quite refractory to anticonvulsant therapy. Focal nonconvulsive or convulsive status epilepticus can be seen as well, requiring video or continuous EEG monitoring for closer surveillance.

Voltage Gated Potassium Channel (VGKC) Complex-Associated Antigens / Leucine-rich glioma inactivated protein (LGI1)

Limbic encephalitis, inclusive of autoantibodies to VGKC and non-paraneoplastic LGI1 protein, predominately present with subacute onset of recent memory loss, behavioural changes, seizures, myoclonus and syndrome of limbic encephalitis[23,24]. Subtle clinical features of depression and anxiety, and sleep disturbances including insomnia and REM sleep behaviour disorder over the weeks to months may be the clinical presentation[25]. In addition to neuroradiology and CSF analysis, EEG is useful in supporting the diagnostic criteria for autoimmune limbic encephalitis as it will show epileptic discharges and slow wave activity predominately over the temporal regions in this patient cohort. MRI may show hyperintensities in the mesial temporal lobes reflecting neurophysiology findings. In 10% of patients a thymoma may be present. Biochemically, the patient may be hyponatraemic. Treatment involves immunosuppression and often there is only partial response to this.[23,26]

Creutzfeldt-Jakob disease

Creutzfeldt-Jakob disease (CJD) is a rare and fatal prion disease also known as transmissible spongiform encephalopathy (TSE). Prion diseases are neurodegenerative diseases that have long incubation periods. The pathology of CJD commences with neuronal loss followed by proliferation of glial cells. There is a presence of small vacuoles within the neutrophils with an absence of an inflammatory response[4].

Several types of CJD have been identified including sporadic, familial, variant and iatrogenic.

Initial psychological symptoms of CJD may include: severe depression, intense feelings of despair , social withdrawal, anxiety, irritability and insomnia. To diagnose CJD the patient will present with a progressive dementia and at least two out of the following four clinical features: myoclonus, visual or cerebellar disturbance, Pyramidal/extrapyramidal dysfunction or akinetic mutism.

Investigations and diagnostic indication for CJD will include:

- A typical EEG pattern inclusive of generalised periodic sharp wave complexes which are of about 1Hz or greater.
- Positive 14-3-3 CSF assay
- MRI high signal abnormalities in caudate nucleus and/or putamen
- With a clinical onset to death of less than two years

In sporadic CJD, the normal electrical rhythms of the EEG are gradually lost. In the majority of cases generalised bi- or triphasic periodic sharp wave complexes appear with a frequency of around 1-2Hz. This pattern tends to develop throughout the course of the illness and, in some cases, may not appear until extremely late. Therefore, finding a positive EEG may require repeat studies. 60 – 80% of cases of sporadic CJD will eventually develop the characteristic periodic picture[14].

Conclusion

In summary, differentiating whether a condition is psychogenic or neurological in aetiology is critical and as we have described, many presenting features overlap. For those presenting with neuropsychiatric symptoms it is evident that EEG/EMG/NCS and EPs are useful tools in aiding diagnosis and guiding management strategies. A wide range of pathologies from neurodegenerative, autoimmune, infective, and structural can be diagnostically supported by neurophysiology testing. Through testing, the differentiation between organic and non-organic pathologies, and epileptic and non-epileptic presentations can be clarified. The development of point of care EEG, where EEG will be used for example in the emergency room to differentiate non-epileptic versus epileptic attacks, is likely to remove much of the associated morbidity related to prolonged intensive therapy unit stays for patients who in fact have non-epileptic events.

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