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NEUROLOGICAL INVESTIGATIONS

# Electroencephalography

C D Binnie, P F Prior

## Genesis of the electroencephalogram

The electroencephalogram (EEG) is a recording of cerebral electrical potentials by electrodes on the scalp. Cerebral electrical activity includes action potentials that are brief and produce circumscribed electrical fields, and slower, more widespread, postsynaptic potentials. The magnitude of the signal recorded from a neural generator depends on the solid angle subtended at the electrode. Consequently, the activity of a single neuron can be recorded by an adjacent microelectrode, but not at a distant scalp electrode. Synchronous activity in a horizontal laminar aggregate of neurons with parallel orientation may, however, constitute a generator of sufficient extent to be detectable on the scalp. Thus the EEG is a spatiotemporal average of synchronous postsynaptic potentials arising in radially oriented pyramidal cells in cortical gyri over the cerebral convexity. It is estimated that the smallest detectable generator has an extent of some 6 cm.[2] Tangentially oriented generators in the walls of sulci do not generally appear in the EEG, but are seen in recordings of the brain's magnetic field (magnetoencephalogram (MEG)).[1]

Synchronous neuronal activity arises by various mechanisms. Isolated aggregates of interconnected neurons spontaneously adopt rhythmic synchronous firing patterns. Afferents—for instance, from the reticular formation—stimulate individual neurons into independent asynchronous activity. Thus synchrony is reduced by arousal and cognitive activity and increases with reduced vigilance, both in normal sleep and in pathological states, reflected in the EEG by increased amplitude and slowing. Specific pacemakers also exist that produce rhythmic synchronous activity.[2] There is, for example, an inhibitory feedback loop involving thalamocortical neurons that produces oscillatory burst firing in drowsiness and sleep. Transitory synchronous activity can be elicited by afferent stimuli (evoked potentials), spontaneous arousal (producing such phenomena as vertex sharp transients in light sleep), and pathological neuronal discharges in epilepsy.

## Interpretative principles

Abnormalities on the EEG reflect general pathological processes and are rarely of specific diagnostic significance. Thus slowing may arise from causes as diverse as cerebral oedema or hypoxia, or systemic disorders such as hepatic insufficiency. The most reliable abnormal EEG sign is reduction of normal activity, ranging from reduced amplitude over a past cerebral infarct or a subdural haematoma, to electrocerebral silence in brain death. Spiky waveforms (epileptiform activity) occur in epilepsy and in some patients with cerebral disorder but without seizures. Rhythmic slow activities may occur bilaterally over the frontal or posterior temporal regions in patients with dysfunction of diencephalic or brainstem structures.

The EEG is profoundly influenced by alterations in vigilance and also changes with age, most noticeably during childhood. Interpretation must take account of the range of normal findings at different ages and in different states of awareness. The slower components diminish with maturation and increase in sleep and drowsiness. As slowing is a common EEG abnormality, it may be difficult to distinguish the effects of immaturity, drowsiness, and pathology. This similarity between the immature and the abnormal EEG underlies an interesting approach to quantitative clinical EEG analysis by Matoušek and Petersén.[3] They developed a method of computing the patient's apparent age from spectral features and used the ratio of calculated to actual age as a measure of EEG abnormality.

## Electroencephalography technology

### DEVELOPMENTS

Traditionally EEGs were written on electromechanical chart recorders; these are now being replaced by digital systems, which offer improved reliability and compact, accessible archives on optical discs. Within a few years clinical neurophysiology laboratories will be based on a local computer network, probably with generic data acquisition stations for recording EEG, EMG, and evoked potentials directly on to a file server, and workstations for reviewing the data and entering reports to form an integrated archive with the original signals.

These innovations have done little to reduce the inherent technological difficulties of obtaining satisfactory recordings of the EEG which, having an amplitude of only

**Department of Clinical Neurophysiology, The Maudsley Hospital, Denmark Hill, London SE5 8AZ, UK**
C D Binnie

**Department of Clinical Neurophysiology, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE, UK**
P F Prior

Correspondence to:
Dr C D Binnie.

some 5 to 200 $\mu$V, is very susceptible to artifacts, from both bioelectric and physical sources. The problems can be largely overcome by good electrode technique, but this is particularly difficult to achieve in children and in others who may be distressed and uncooperative. Methods of constructing electrodes have changed little in recent decades, but a significant advance has been the development of improved adhesive pastes, which achieve secure electrode fixation and a low contact resistance without abrasion of the skin—an important consideration given current concerns with avoidance of cross infection.

Changes in vigilance may affect the occurrence of pathological phenomena; particularly in epilepsy, clinically relevant abnormalities may be found in sleep but not in wakefulness. Sleep recording is generally underused and is not routinely available in many departments.

### EPILEPSY MONITORING

Arguably the most important recent development in epileptology has been long term EEG and video monitoring (see Binnie[4] and Gotman *et al*[5] for reviews). As the manifestations of epilepsy are intermittent, a routine EEG often fails to show epileptiform activity, which may occur only during seizures. Moreover, interictal epileptiform activity may be of doubtful clinical value, either for identifying the site of onset of seizures or for determining whether particular clinical events are epileptic.

The EEG can be telemetered over days through a cable or radio link, permitting limited mobility in hospital, while behaviour is documented by video. Alternatively, ambulatory monitoring can be carried out in an everyday environment with a portable cassette recorder, but behavioural documentation will be less reliable, depending on reports of carers. These technologies have different applications; telemetry is generally preferred, unless it is essential to record in a particular environment.

### BRAIN MAPPING

A technical development that has generated recent enthusiasm is brain electrical activity mapping. Computer assisted EEG analysis has been used in research for more than 30 years, but has few clinical uses beyond monitoring (during surgery and intensive care and in metabolic disorders) and for automatic seizure detection during telemetry. Quantitative EEG information may be displayed topographically on a stylised head outline.[6-8] With development of personal computers these facilities have become commercially available and widely promoted for clinical use. The colourful displays invite comparison with neuroimaging, misleadingly, as EEG topography does not bear a simple relation to pathology. Artifacts are readily overlooked or generated in the process of analysis and mapping. Brain mapping extends expert analysis of the primary data,[9] and may highlight features that are difficult to detect,[10 11] but its general clinical utility has yet to be established and its promotion as a substitute for conventional EEG can only be deplored.[12 13]

## Cerebral lesions

Electroencephalography provides information that primarily concerns disturbances of function rather than structure. Whereas clinical studies in the 1930s showed localised changes at the site of cerebral mass lesions, routine referral for EEGs on suspicion of intracranial tumour is no longer appropriate. Modern imaging techniques, although somewhat more costly, provide more precise identification of the presence, nature, and site of such lesions. It should also be noted that in this context the value of a negative EEG in excluding pathology may be somewhat illusory. The normal EEG does not exclude intracranial disorders; a more appropriate approach to the investigation is to recognise the significance of EEGs with positive findings. The EEG only plays a relevant part when patients cannot, for various reasons, undergo scanning or when potential epileptogenicity,[14] possible postoperative recurrence of a tumour, or toxic effects of medical oncological drugs *v* metastatic disease require evaluation. In these situations, clinical value accrues in the evolution of changes over serial recordings.

Vascular lesions may be more rewarding to investigate than tumours. The changes after a cerebral infarct will be most characteristic in the first hours and days, before those on CT become evident. Typically the appearances are of a localised reduction of normal cortical rhythms and a major surrounding slow wave abnormality with individual waves of less than 1 Hz. There is often a rapid evolution of the EEG abnormality that may resolve before the scan becomes positive.

Prognostic assessment of CT negative patients with transient or mild ischaemia depends on subtle abnormalities evident only when quantitative EEG techniques are used. These utilise computer analysis of the EEG frequency spectrum. A sensitivity of 50–70% and a specificity of 90–100% have been reported.[15-17] The topic is thoroughly reviewed by van Huffelen,[18] who also reminds us of the value of quantitative EEG techniques and somatosensory evoked potentials in monitoring patients at risk of cerebrovascular accidents during carotid[19 20] or open heart surgery.

Head injury is another condition where the detection of lesions by EEG has been rightly superseded by imaging, although its use for prognostication during coma has increased.[21 22] Quantitative methods, as with ischaemic lesions, can distinguish patients after mild head trauma from controls.[23]

Two groups of EEG phenomena in patients with cerebral lesions—periodic events and projected rhythms—sometimes cause confusion. The fascinating and distinctive range of periodic EEG phenomena merits particular attention. Periodic lateralised epileptiform discharges (PLEDs) are acute, self limiting features with a repetition rate of 3–7 per 10 second period that reflect a sudden

disturbance of blood supply at or near the cortex or cortical white matter junction.[24] They occur in obtunded patients, varying with fluctuations in consciousness, tending to decrease when the patient is alerted. The PLEDs are not specific to any particular pathology (but confirm that local pathology is present), being seen with extracerebral haematomas, metastases, infarcts, infections, etc. They run a one to two week course, disappearing even when the underlying lesion is progressive. Although described as epileptiform, any focal clinical events may be subtle and transient. The PLEDs may be bilateral—for example, in herpes simplex encephalitis when they evolve with different periodicity over each temporal lobe. They appear, often unilaterally, on the second or third day of the illness, and become evident contralaterally by the next day. The independent timing or repetition rate of the PLEDs over each hemisphere is an important diagnostic feature in herpes simplex encephalitis, implying separate localised areas of pathology arising in the temporal lobes rather than a generalised encephalitic disorder. If PLEDs arise elsewhere—for example, in frontal or parietal regions—they should be interpreted with caution: most patients turn out to have other pathology. The EEG in herpes simplex encephalitis shows a parallel, progressive, loss of normal cortical rhythms and may show prolonged seizure discharges waxing and waning over one or other temporal lobe, with or without clinical accompaniment. With antiviral agents, PLEDs can resolve rapidly; it is thus important to consider the value of an emergency EEG to establish the likely diagnosis at an early stage before antibody titres become available.

Generalised periodic discharges in the EEG occur in subacute sclerosing panencephalitis in children and teenagers and in Creutzfeldt-Jakob disease in the middle aged. In subacute sclerosing panencephalitis the discharges may be subtle initially and consist of simultaneous bilateral complexes of slow and faster components, each stereotyped morphologically in a particular region, repeating at about 10–20 second intervals. By contrast, those of Creutzfeldt-Jakob disease occur at about 1–2 second intervals and are more likely to be confused with ECG pickup on the scalp. In both conditions there is a gradual loss of cortical rhythms until the repetitive complexes appear on a near silent background. Periodic EEG complexes have not been found in Kuru; they were also absent in the 46 patients with progressive dementia and myoclonus considered as possible Creutzfeldt-Jakob disease but in whom neither transmissibility nor prion protein could be demonstrated.[25] Similarly, in Gerstmann-Sträussler-Scheinker disease periodic complexes are limited to patients with clinical manifestations resembling Creutzfeldt-Jakob disease.[26] Although associated with spectacular EEG changes at a fairly early stage (often before the conditions have been considered diagnostic possibilities), Creutzfeldt-Jakob disease and subacute sclerosing panencephalitis are rarities. More common causes for generalised periodic EEG features are mentioned with the systemic disorders.

The projected rhythms or socalled "rhythms at a distance" are another potential cause of confusion when assessing EEG reports. As already described, cortical rhythms are generated locally but modulated by deeper pacemakers at both thalamic and brainstem reticular activating system levels. Lesions or biochemical dysfunction in subcortical structures may produce projected effects on the EEG via thalamocortical and other pathways. Two forms of projected abnormality are commonly encountered and have somewhat different mechanisms.

The first is the paradoxical slow wave arousal response[27] in which a noxious stimulus in a lightly or moderately comatose patient produces a massive and prolonged run of slow delta activity starting at less than 1 Hz and gradually increasing in frequency. It may last for several minutes and be accompanied by tachycardia, tachypnoea, increase in arterial blood, and intracranial pressures and motor activity ranging from a few muscle potentials on the ECG or EEG tracing to a massive extensor decerebrate response. It represents an abnormal arousal response, most commonly due to dysfunction or damage to the brainstem reticular activity pathways. It is common in young people comatose in the first week after head injury and, although it indicates a reason for slow awakening from coma, it does not necessarily carry a poor prognosis.

The second type of projected slow wave abnormality, frontal intermittent rhythmic delta activity (FIRDA), and its occipital counterpart (generally confined to childhood or the early teens), are rhythmic bursts of bilaterally synchronous delta waves at 2 Hz that are attenuated on alerting the patient or on eye opening to command. They occur in metabolic or toxic disturbances and also with intracranial lesions involving or compressing subcortical structures.

The metabolic causes of FIRDA may be as benign as the typical response to routine "voluntary" hyperventilation in the healthy young subject during EEGs or reflect, for example, a serious disturbance of calcium or glucose metabolism. A typical toxic cause for this EEG pattern is phenytoin toxicity.

Intracranial lesions producing FIRDA include subdural haematomas, carotid occlusion, frontal or subfrontal or callosal "butterfly" tumours, thalamic lesions, and basal infiltrations or exudates (for example, tuberculous meningitis). Evolution may be complex from lateralised or asymmetric, to symmetric, then contralateral as, for example, a butterfly tumour grows across the midline.

Distinguishing between intracranial lesions and encephalopathies when FIRDA presents the main EEG abnormality rests on careful inspection of both the delta bursts and the background on which they appear.

## Epilepsy

PATHOPHYSIOLOGY

Epilepsy is characterised by excessive and hypersynchronous neuronal activity. Synchronous activity in a small neuronal aggregate at the onset of a partial seizure is often of high frequency (12–70 Hz) and may be recordable only by depth electrodes.[28] As larger populations are recruited, slower, rhythmic, spiky activity appears more widely, often showing a progressive increase in amplitude and diminution of frequency, and may be detected with EEG electrodes on the scalp. In generalised seizures, or after propagation of those of focal origin, normal thalamocortical oscillatory burst firing mechanisms[29] may be entrained, producing repetitive spike wave activity,[30] recordable both over the cortex and in the thalamus. The spikes correspond to burst firing, the slow waves to periods of reduced neuronal activity due to hyperpolarisation of thalamocortical cells.

In the interictal state similar activities may briefly occur. Apart from generalised spike and wave activity, however, interictal discharges are generally slower and of greater amplitude than early ictal events. Interictal EEGs of patients with temporal lobe epilepsy thus typically show discrete anterior temporal spikes and sharp waves, unlike the faster, rhythmic activities at seizure onset.

Electrophysiological findings have contributed importantly to theoretical concepts and classifications of epilepsies and seizures, supporting for instance the central distinction between localised and generalised corticoreticular epileptogenesis.[31 32] Indeed the main clinical application of the EEG in epilepsy is for classification. It is, for instance, of practical use to distinguish the focal discharges of partial epilepsy from generalised epileptiform activity. As focal ictal and interictal events can undergo rapid propagation leading to secondarily generalised discharges and seizures, it is important to identify possible focal elements at the onset of a generalised discharge. The EEG also contributes to classification by detecting abnormalities of ongoing activity due to cerebral pathology, focal slowing, or asymmetries of normal activity in symptomatic partial epilepsy, and generalised abnormalities in symptomatic generalised epilepsy.

Spikes, sharp waves, and spike and wave activity are seen in some patients with cerebral disorders without epilepsy. There is no agreed name for this class of EEG phenomena; the phrase, "epileptiform activity", used here, acknowledges the association with epilepsy underlying the concept, while stressing that the term refers to the waveform, not its clinical correlates. Various sharp or episodic transients occur in normal subjects and are a source of misunderstanding. They are recognisable by characteristic waveform, topography, and circumstances of occurrence and should not be mistaken for phenomena supporting a diagnosis of epilepsy.[33 34] Most often misinterpreted are 6 and 14 per second positive spikes, rhythmic bursts which, unlike most epileptiform activity, are electropositive at the site where they are of greatest amplitude. They occur in many adolescents and young adults during drowsiness and light sleep and are not associated with epilepsy. Other non-epileptic spiky or episodic phenomena include benign epileptiform transients of sleep (short sharp spikes), rhythmic midtemporal discharge (formerly misleadingly termed psychomotor variant), and the bifrontal slow activity seen on hyperventilation in normal children, which too often is wrongly interpreted as evidence of epilepsy.

*Table 1 Misconceptions about the EEG in epilepsy*

| It is not in general true that: |
|---|
| • The interictal EEG can: |
| Prove the diagnosis of epilepsy |
| Exclude epilepsy |
| • An ictal EEG almost always shows: |
| Epileptiform activity |
| Any other change |
| • EEG abnormality reflects severity as manifest by: |
| Seizure frequency |
| Therapeutic response to AEDs |
| Prognosis |

*Table 2 Utility of EEG in epilepsy*

| The interictal EEG is of value to: |
|---|
| • Support diagnosis if other cerebral disease can be excluded |
| • Exclude or identify specific epilepsy syndromes |
| • Classify epilepsies and syndromes |
| • Detect or confirm photosensitivity |
| • Detect non-convulsive status epilepticus |
| • Detect antiepileptic drug intoxication |
| • Detect possible epileptogenic lesion |
| • Monitor status epilepticus |
| • Locate epileptogenic zone in preoperative assessment by ictal recording |
| Ictal recording, by long term monitoring if necessary, is of value to: |
| • Distinguish epileptic from non-epileptic attacks |
| • Classify seizures |
| • Determine incidence of frequent minor seizures |
| • Detect subtle seizures including transient cognitive impairment |
| • Identify seizure precipitants including self induction |

DIAGNOSTIC STRATEGIES

Such interpretative errors contribute to confusion about the sensitivity, specificity, and general utility of the EEG (tables 1, 2). Most routine EEGs are interictal and attention focuses chiefly on epileptiform activity. The EEGs of people with epilepsy show considerable spontaneous variation, however, and may exhibit interictal discharges on one occasion and not on another. Serial studies indicate that only one third of patients with epilepsy consistently exhibit discharges in the interictal, waking state; one sixth never do so; in the remaining half the picture varies, with a probability of about one in three of epileptiform activity in any 30 minute waking record.[35] Drowsiness and sleep increase the probability of finding discharges, particularly in partial epilepsies.

These considerations suggest strategies for EEG investigation of epilepsy. Possibly as routine, certainly if an initial waking record shows no epileptiform activity, a sleep tracing should be obtained. The combination of a waking and sleep EEG shows epileptiform activity in 80% of adults with epilepsy and in a larger proportion of children. With repeated

waking and sleep records the number approaches 92%.[36] If the interictal EEG is persistently negative and a clinical problem exists that may be resolved by EEG evidence, an ictal recording may be obtained by telemetry, provided that the seizures are often enough to be captured within a reasonable period.

Regarding specificity of epileptiform activity to epilepsy, estimates of false positives are inflated by misinterpretation of the non-epileptic transients noted earlier. In neurologically screened adults the prevalence of rigorously defined epileptiform activity is some 3/1000[37 38]; comparable data for children are not available but the prevalence is probably higher. Clinical EEG investigations are, however, performed not in normal subjects, but in patients with symptoms of possible cerebral origin. Here the incidence of EEG abnormalities, including epileptiform activity, is much greater.[39] Overall 10% of patients who have undergone intracranial surgery and 3% of psychiatric patients without epilepsy exhibit epileptiform EEG activity.[40] The interpretation of a record containing spikes depends therefore on the clinical context. This finding, in a patient with mental handicap or a cerebral tumour, contributes little to the diagnosis of epilepsy. Conversely, the finding of epileptiform discharges in a patient with episodic symptoms and without evidence of cerebral pathology shifts the balance of probability in favour of epilepsy.

Due in part to spontaneous variation of the EEG, a close relation is rarely found between the amount of epileptiform activity in routine records and current seizure frequency or response to medication. Repeated EEGs are, however, requested in the belief that they are of value for monitoring clinical progress.[41] Similarly, the EEG is of little value for deciding when to terminate medication in adults who have become seizure free[42] except in so far as it reflects different syndromes with different prognoses. In children, however, persistent epileptiform activity indicates a high probability of relapse.[43 44]

## ACTIVATION PROCEDURES

The importance of EEG activation by sleep has already been noted. Spontaneous sleep can often be achieved by a restful recording environment and a relaxed approach. Sleep can also be induced by medication or by prior deprivation of sleep. Sedative drugs modify the EEG, producing increased fast activity, but this is no disadvantage as it may highlight any local reduction of fast activity reflecting underlying pathology. Sleep deprivation increases seizure liability but there is little evidence that it specifically activates the EEG except by promoting sleep.[45] It is usually more convenient to induce sleep by medication than by sleep deprivation.

Two other activation procedures are routinely used: hyperventilation and photic stimulation. Three minutes of vigorous overbreathing induces a seizure accompanied by spike and wave activity in patients with absences, so consistently that the lack of such a response virtually excludes uncontrolled absence epilepsy (but not other epilepsies).[46] Other types of EEG abnormalities and seizures are less consistently provoked.

Rhythmic photic stimulation elicits generalised, self sustaining epileptiform discharges in some 5% of people with epilepsy, particularly in those with idiopathic syndromes, notably juvenile myoclonic epilepsy.[47 48] Photosensitivity is of practical importance: most photosensitive subjects found in clinical EEG practice have epilepsy[49] and have seizures induced by environmental visual stimuli such as television and flickering sunlight. In about 50% it seems that no spontaneous seizures occur, all attacks being visually induced.[47 50] Avoidance of precipitating stimuli rather than medication is an important therapeutic option.

## MONITORING

Long term monitoring is most used for differential diagnosis of epileptic and non-epileptic attacks.[51 52] The presence of ictal EEG changes will generally confirm the epileptic nature of an event (as cardiogenic seizures also produce EEG changes, simultaneous ECG monitoring may be necessary).[53] Interpretation of a negative ictal EEG may, however, be difficult. Abnormal activity in small or deep neuronal populations may not be reflected in the EEG, or may produce only minor changes in ongoing rhythms. Various different seizure types are consistent in this respect. Absences, for instance, are accompanied by spike and wave activity; a staring attack without this cannot be an absence. The EEG signatures of some seizure types are usually not epileptiform: low amplitude fast activity occurs during tonic seizures, an electrodecremental event during an infantile spasm, or an atonic seizure, and bitemporal theta activity during many complex partial seizures. Simple partial seizures, particularly with psychic or viscerosensory symptoms, often produce no EEG change.[54] Interpretation of an apparently negative ictal EEG thus depends on the nature of the seizure and coregistration of the EEG and behaviour to facilitate detection of minimal EEG changes.

Close comparison of the EEG with behaviour may also show subtle ictal events, or show these to be more frequent than supposed.[55 56] Thus a momentary arrest of activity may be identified as ictal because of consistent accompanying EEG change. Conversely, seemingly interictal EEG discharges may be shown to be accompanied by subtle clinical events. If no changes are evident during unconstrained behaviour, transitory cognitive impairment may be shown by more structured tasks, including formal psychological testing.[57] This is a possibility to be considered in any patient with frequent EEG discharges and unexplained cognitive difficulties.

Ictal recording, sometimes with foramen ovale,[58] subdural, or depth electrodes,[59–61] forms an important component of preoperative assessment as an aid to identifying the site

of seizure onset. Here too, simultaneous behavioural monitoring is essential, as electrographic localisation of seizure onset cannot be claimed if clinical events precede the first detected electrical changes.

Ambulatory monitoring without video documentation of behaviour is not a substitute for telemetry in detecting minor seizures, locating ictal onset, or deciding whether subtle events are epileptic. It is, however, the preferred method for investigating a known EEG phenomenon in a particular setting—for instance, to determine the frequency of absence seizures at school.

## Psychiatry

Ironically, although the human EEG was discovered by a psychiatrist, and many pioneering EEG laboratories were in psychiatric hospitals, the contribution of the EEG to psychiatry has proved disappointing. Quantitative EEG analysis (and particularly cognitive evoked potentials) tantalisingly show group differences between patients with various psychiatric disorders, their relatives, and control populations. These features generally fall within the range of normal variation, are difficult to detect except by computer assisted analysis, and have no diagnostic value in the individual patient.

### PSYCHOSES

In the functional psychoses there may be group EEG differences from controls or changes with clinical state. Amount and frequency of alpha activity are decreased in depression and increased in mania.[62–64] There is generally a raised incidence of non-specific EEG abnormalities in bipolar affective disorder.[65] Schizophrenic patients typically exhibit low amplitude irregular EEGs, aptly described as "choppy" by Davis,[66] but these too fall within normal limits resembling records of anxious, healthy subjects. Findings of positive diagnostic value by EEG are confined to those psychiatric syndromes with an overtly organic basis.

### CONFUSIONAL STATES

Delirium can be distinguished from psychoses presenting with disturbance of consciousness (for example, mania, acute schizophrenia, and puerperal psychosis) by the finding of EEG abnormalities, which increase with clinical deterioration (table 3). In organic confusional states the EEG typically shows progressive slowing: firstly, reduced alpha frequency, then increasing theta and loss of alpha and beta activity, then diffuse or bifrontal delta activity with onset of coma. The differential diagnosis includes toxic and metabolic disorders (notably hypocalcaemia and hypercalcaemia, hepatic encephalopathy, metabolic alkalosis, and water intoxication—which may occur in schizophrenia), overdosage with psychotropic drugs, and meningitis. Widespread excessive fast activity occurs in delirium tremens[67] and benzodiazepine or barbiturate intoxication. Epileptiform activity, generalised or focal, appears virtually continuously in non-convulsive status epilepticus, and intermittently, often in association with photosensitivity, after acute withdrawal of barbiturates, alcohol, or benzodiazepines.

*Table 3 EEG in acute delirium*

| |
|---|
| Slowing: consider—infective, toxic, or metabolic cause, including drug overdose |
| Excess fast activity: delirium tremens or tranquiliser overdose |
| Continuous epileptiform activity: non-convulsive status epilepticus (confirm by EEG response to IV diazepam) |
| Unexplained intermittent epileptiform activity especially with photosensitivity: drug or alcohol withdrawal |
| Normal: psychiatric cause most likely but repeat EEG if condition deteriorates |

### DEMENTIA

The commonest organic differential diagnosis in old age psychiatry is between the vascular and various non-vascular dementias, and the commonest organic and functional differential diagnosis is between the various dementias and depressive pseudodementia. A normal EEG is compatible with any dementia, especially early in the condition and serial recording is therefore often required. In Alzheimer's disease,[68 69] there is early decrease in alpha frequency and amplitude; later generalised irregular slow activity appears with a frontal emphasis and fast activity disappears. Serial quantitative EEG studies show a high correlation between the degree of dementia and theta power and mean frequency.[70] Focal EEG changes, with or without generalised slowing, suggest either multi-infarct dementia[71] or normal pressure hydrocephalus.[72]

Among the less common dementias, Huntington's chorea is characterised by a tracing of conspicuously low amplitude; this is of little clinical value, being rarely seen in atypical or early cases.[73 74] Changes in the EEG are uncommon and mild in alcoholic dementia[75] and in Pick's disease,[76 77] contrasting with the severe clinical picture. In the course of Creutzfeldt-Jakob disease, diffuse or focal slowing develops, with characteristic stereotyped, bilaterally synchronous sharp waves. Regular slow triphasic bursts on slow background activity usually appear at advanced stages.[77] Serial recordings when awake and sleeping may be required to detect these but it is claimed that if periodic discharges have not appeared within 10 weeks a diagnosis other than Creutzfeldt-Jakob disease is unlikely.[78] Later the record consists of diffuse slow activity of progressively diminishing amplitude.[79]

### CEREBRAL TUMOUR AND PSYCHIATRY

Before the advent of neuroimaging the yield of unsuspected cerebral tumours from routine EEGs in psychiatric hospitals was about 1%.[80] Abnormal findings were not uncommon but mostly mild, non-specific, and often inexplicable (possibly iatrogenic), rarely providing evidence of localised structural abnormality. Now, with appropriate use of CT, the contribution of EEG to the detection of lesions underlying psychiatric symptoms should be

negligible. Meningiomata are over represented in psychiatric patients, however, and often present with epilepsy; occasionally EEG investigation of a patient with atypical auditory or olfactory hallucinations with absent or atypical psychotic symptoms will lead to the detection of a tumour.

POST-TRAUMATIC SYNDROMES

A range of psychological disabilities and psychiatric conditions occurs after head injury, particularly in cases of post-traumatic epilepsy.[81] Late EEG changes are not closely related to the chronic psychiatric morbidity after head injury. After brain injury the affected neurons either die or recover and the EEG then becomes normal apart from possible amplitude reduction or changes related to epilepsy. Paradoxically, a normal EEG is an adverse sign: post-traumatic symptoms that remain after the EEG returns to normal are likely to persist.[82]

EPILEPSY AND PSYCHIATRY

Preictal or postictal EEG changes may elucidate the relation between seizures and psychiatric symptoms in patients with psychoses associated with epilepsy. Rarely, the finding of epileptiform activity establishes unrecognised epilepsy as a cause of psychiatric symptomatology—for instance, in the Landau-Kleffner syndrome. There are often requests for EEGs to investigate epilepsy as a possible cause of episodic behavioural disturbances in mentally handicapped children, or of hallucinosis in patients likely to be psychotic. Such investigations rarely serve any useful purpose unless performed during the behaviour in question, and in any event the yield of diagnostically useful information is small.

## Sleep

The EEG is probably the most sensitive measure available for detecting changes in alertness. It changes profoundly during sleep, has played an important part in the development of concepts concerning sleep, and is an essential component of accepted sleep staging systems. That described by Dement and Kleitman[83] has been employed for almost 40 years, generally by experienced observers with standardised rating criteria. Automatic or more usually computer assisted sleep staging systems are now available, making quantitative sleep studies less labour intensive and more accessible as clinical and research tools. As well as the classical stages of light, deep, and rapid eye movement (REM) sleep, other patterns have been recognised, notably the cyclic alternating pattern of deep and lighter sleep with a period of only 40 seconds.[84] This in turn is related to other regulatory mechanisms and there is hope that it may be of value in the investigation of, for instance, cardiac and autonomic dysfunction.

Sleep provides a valuable means of activating the EEG to obtain clinically significant information—for instance, to elicit epileptiform activity—as noted earlier. In various encephalopathies, even without seizures, characteristic EEG abnormalities may appear more readily during sleep, at certain phases of evolution of the disease. Thus sleep recording may be necessary to show the repetitive complexes of Creutzfeldt-Jakob disease and of subacute sclerosing panencephalitis, particularly in the early stages.

EEG recording during sleep has a special role in the investigation of the dysomnias and parasomnias. For nightlong "polysomnography" in patients with possible disturbances of ventilatory function, the EEG is recorded in combination with other variables—namely, EMG, ECG and oculogram, oxygen saturation, air flow, and thoracoabdominal movement. These are required for sleep staging or investigating ventilatory disturbances.

Polysomnography, including respiratory studies and sleep oximetry, has a major role in the investigation of sleep apnoea and during the establishment of treatment with continuous positive airway pressure. Sleep apnoea is common, with a prevalence variously estimated as 1 to 10%.[85 86] Oximetry alone may be adequate to identify more than 50% of patients,[87 88] but in many patients with a high clinical suspicion of the condition, oximetry results are equivocal or normal, and polysomnography is then necessary for proper evaluation. The condition of high upper airway resistance is characterised by snoring and frequent arousals but without apnoea and here polysomnography is essential for diagnosis. Although costly and not widely available, nocturnal polysomnography is therefore the most satisfactory method of investigating patients with diurnal drowsiness or who report unexplained sleep disturbances.[89] Unlike oximetry alone, it will also help to identify those whose symptoms have some other cause, such as nocturnal epileptic seizures.

For investigation of sleepiness, notably in such conditions as narcolepsy, the multiple sleep latency test is used. The subject is repeatedly placed in a quiet dark environment during the daytime and allowed to fall asleep. The mean time to onset of sleep provides a measure of sleepiness (five to 10 minutes represents moderate, and less than five minutes, severe sleepiness). In addition, the electrophysiological pattern at sleep onset is noted. In normal subjects there is a gradual progression through sleep stages of increasing depth, whereas in narcolepsy, and rarely in subjects with sleep apnoea, there may be a rapid progression to deep sleep or to the REM stage, not normally seen until after some 90 minutes of sleep. In many sleepy patients both nocturnal polysomnography and a multiple sleep latency test will be required for a full evaluation.

## HIV and AIDS

Both HIV infection and full blown AIDs present a new range of neurodiagnostic problems. With strict assessment criteria, it seems that EEGs are normal in patients infected

with HIV who have unimpaired neuropsychological status.[90] In those with AIDs or AIDs related complex, the incidence and severity of abnormal EEGs increased with development of AIDs related dementia, 65% showing diffuse and 22% focal slowing, and 11% paroxysmal slow and sharp activity.[91] Current patterns of disease and use of prophylactic treatment against infections are associated with a preponderance of diffuse encephalopathic EEG abnormalities over focal changes from localised lesions or multifocal leucoencephalopathies. Diffuse slowing is correlated with slowed reaction times[92] and, together with quantitative methods in longitudinal studies, provides a sensitive warning of impending neurological disease in asymptomatic patients.[93]

## Systemic disorders

The encephalopathies form an indication par excellence for systematic EEG studies and use of simple quantitative methods. In general terms there is a fairly consistent sequence of global EEG changes, often quantitatively related to the severity of the underlying metabolic or toxic process. These comprise slowing of the normal ongoing posterior (alpha) rhythm, gradual loss of its reactivity to eye opening or auditory stimulation, further slowing to theta and delta frequency ranges with loss of faster components, then a terminal state in which intermittent suppression of activity progresses to total electrical silence.

With certain exceptions, such as the triphasic waves of hepatic precoma and coma, there are few specific EEG features and the contribution of the investigation is to indicate the presence and severity of abnormality rather than a particular diagnosis. This is especially important in the confused patient for distinguishing between an organic cause such as an encephalopathy, non-convulsive status epilepticus (which may even mimic hepatic encephalopathy with repetitive stereotyped diphasic or triphasic complexes), and some psychogenic causes.

The consistent sequential EEG changes in metabolic and toxic encephalopathies, their quantitative relation to severity of causal factors, their independence of patient responses, and their objective nature, provide valuable clinical tools. This has led to the development of various electronic methods for measurement of EEG changes.[94] The value of such methods is in the rapid and continuing feedback to the clinician for guidance in management—for example, in an acute crisis where complex medical or surgical intervention may be required.

Exclusion of an acute or subacute encephalitic illness may be a reason for the EEG in a patient admitted in coma with little available history concerning antecedent events. Repetitive EEG transients may occur in encephalitis, but also unfortunately with several alternative conditions such as hepatic encephalopathy ("triphasic waves"; see Fisch and Klass[95] regarding diagnostic specificity), severe post hypoxic encephalopathy, and occasionally in uraemia, electrolyte disorders, and barbiturate overdose.

Whereas acute cerebral hypoxic damage leads to diffuse repetitive transients, an episode of profound arterial hypotension or perfusion failure usually produces changes localised to arterial boundary zone or "watershed" regions.[96] These may include PLEDs together with local flattening and surrounding localised slow waves. Such changes may also occur with raised intracranial pressure, or when hypotension occurs in patients with occlusive vascular disease in the neck. Apart from causal attribution, differentiation between ischaemic and hypoxic abnormalities is of clinical importance as outcome in patients with boundary zone infarcts may be improved by reduction of surrounding oedema and control of epileptiform activity.

## Intensive care

The neurophysiology team is closely involved in many aspects of intensive care. Only limited clinical neurological assessment is possible in unconscious, sedated and ventilated, or traumatised patients with problems from inaccessibility of limbs because of traction or vascular lines and impossibility of examining pupils, optic fundi, and caloric responses because of local trauma or swelling. A carefully planned EEG can help by demonstrating a global cerebral response to systematic stimulation in peripheral and cranial nerve territories.

Unfortunately, the EEG itself may be extinguished by major sedatives and anaesthetics commonly used in intensive care units, albeit in higher doses than commonly used in the United Kingdom. In high dose barbiturate treatment of major head injuries short latency evoked potential recordings may provide the only means of knowing if the brain is alive.[97] Conveniently, short latency evoked potentials are not appreciably affected by major intravenous sedative and anaesthetic agents and have predictive value even when the EEG has been rendered isoelectric.[98] Prognosis after severe trauma may be helped by multimodality evoked potential studies,[99 100] and in the absence of significant sedation, scoring systems based upon EEG features retain a useful place.[101]

In hypoxic-ischaemic coma burst suppression patterns and isoelectric EEGs, unless caused by CNS depressant drugs or hypothermia, are of adverse prognostic import. Total EEG silence occurs during asystole but with resuscitation intermittent and then continuous activity return by three and 10·5 hours respectively in patients who will recover from coma.[102] In a comparison of recovery times for brainstem reflexes and EEG in a series of 125 patients, a stereotyped sequence of returning brainstem reflexes preceded the first appearance of EEG activity (from respiratory movements and pupillary light reflex by seven to 12 minutes, to stereotyped reactivity by 3·3 hours). Full recovery was only seen in patients

in whom intermittent EEG had returned within three hours, consciousness within two days, speech within 6·5 days, and activities of daily living by two weeks.[102] Predictors from EEGs, based on systematic scoring compared with a computerised "knowledge-base" derived from patients with established outcome, have long proved powerful tools.[103] Prognostic systems based on quantitative EEG analysis[104] and additional somatosensory evoked potentials[105] extend the basis for prognostic assessment in posthypoxic coma.

Monitoring of severity scores based on EEG features has also proved of prognostic value in sepsis associated encephalopathies when severe but reversible abnormalities occur and require differentiation from effects of major sedatives.[106]

Quantitative EEG methods are presently limited in detection of some prognostically important patterns (for example, FIRDA, triphasic waves, and burst suppression patterns). Indeed, overall patterns of function, including long term cyclic variability and reactivity,[107] are of more fundamental importance than simple quantitative or present or absent measures. Neurophysiological measures are always of much more value when showing positive evidence of function than in assessing possible significance of its absence. None the less despite a wide consensus concerning the primacy of proper clinical testing, there is still occasional controversy over the role of neurophysiological investigations in brainstem death. The arguments for and against are comprehensively reviewed by Chatrian[108] and Pallis.[109]

Purpose built continuous EEG monitoring devices have become a standard part of the intensive care of comatose or sedated patients[110–112] and are used to detect seizure discharges in ventilated patients with status epilepticus,[113] to assist management of sedation in ventilated head injured patients,[114] and in detection of arousals.[115] Now, in addition, evoked potential monitors will allow continuous observation of auditory or somatosensory function to the level of brainstem and primary cortical potentials,[116] some being combined with displays of quantitative EEGs.[117]

The problems of assessing patients in the intensive care unit have been highlighted in a series of nerve conduction and electromyographic studies concerned with difficulties in recovery attributable to myopathies, neuropathies, and neuromuscular problems in the critically ill.[118 119] It is therefore naive to think of EEG as an isolated investigation in unresponsive patients in intensive care units but it may be highly rewarding to approach each individual problem with the appropriate battery of EEG, evoked potential, and EMG diagnostic and monitoring tools.

## Service provision in the United Kingdom

The favoured pattern for optimal delivery of services in the United Kingdom parallels that for other neurosciences, comprising a "hub and spoke" model with the main resources at neuroscience centres, while smaller linked departments in peripheral hospitals provide basic services to local communities. The Association of British Clinical Neurophysiologists[120–122] and the American Electroencephalographic Society[123] have issued recommendations on standards for clinical neurophysiology and guidance to purchasers about the indications for and selection of different investigations. Local services must not be devolved to such a degree that individual departments are too small to be cost effective or to maintain standards. Even a basic EEG laboratory cannot be expected at the site of every neurology outpatient clinic.

An Association of British Clinical Neurophysiologists survey in the four Thames Health Authority regions reported 5500 neurophysiological investigations per million population per annum, more than doubling 1968 levels; EEG comprised half the workload, EMG one third, and evoked potential studies and special techniques the remainder. Two thirds of the investigations were in outpatients; only half the referrals were from neuroscience disciplines, the remainder from other specialties, notably paediatrics, orthopaedics, and rheumatology, but also general medicine, endocrinology, psychiatry, and geriatrics, and other surgical specialties.

The direct cost of a waking EEG is about £70, the total, £100 with ancilliary costs in a neurosciences department. Unit costs will be higher in smaller units. Special EEG examinations range from £200 (drug induced sleep) to £400 per 24 hours for telemetry. Waiting lists for neurophysiology tests now average 4·9 weeks in the United Kingdom (Association of British Clinical Neurophysiologists, 1992–94 surveys). They are longer for procedures requiring active involvement of physicians such as EMG, telemetry, and intraoperative monitoring, and unlikely to fall without an increase in consultant staffing levels.

Diagnostic utility of investigations may be assessed in terms of yield of positive findings or by effect on management. Perhaps not unexpectedly the cost-benefit ratio is most favourable for costly complex investigations considering specific problems such as telemetry,[124] and worst for "routine" examinations used for screening purposes.[41]

## Summary

Notwithstanding recent advances in neuroimaging, EEG remains a major technique for investigation of the brain. Its main applications are in assessment of cerebral function rather than for detecting structural abnormalities. The principal clinical applications are in epilepsy, states of altered consciousness including postanoxic and traumatic coma, the parasomnias, dementias, toxic confusional states, cerebral infections, and various other encephalopathies.

Abnormalities in EEG reflect general pathophysiological processes, raised intracranial pressure, cerebral anoxia, or oedema, epileptogenesis etc, and show little specificity

for a particular disease. Consequently, they need to be interpreted in a particular clinical context; the use of routine EEG examination for screening purposes is rarely of value. Conversely, the investigation becomes most cost effective when applied to specific problems—for instance, monitoring serial changes in postanoxic coma or during open heart surgery, differential diagnosis (by telemetric ictal recordings) of epileptic and non-epileptic attacks, and providing early prediction of outcome after stroke.

High technological standards and an individualised problem solving approach are prerequisites of a cost effective, reliable clinical EEG service. These are most likely to be achieved by a considered, selective referral policy, the use where necessary of prolonged complex procedures such as telemetry, and the avoidance of routine examinations of dubious clinical relevance.


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