The EEG in Coma

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Summary: The EEG allows insight into thalamocortical function in comatose patients when this is inaccessible clinically. A single EEG can help with broad diagnostic categorization whereas continuous or serial EEG provides monitoring for unstable and potentially treatable conditions and for monitoring the effects of therapy. The EEG plays a supplemental role in establishing the prognosis in disease states that are capable of causing neuronal death. The most prevalent and problematic of these conditions involves survivors of cardiac arrest who are initially in coma with intact brainstem reflexes. In such patients single EEGs are of 100% specificity for no possibility of recovery of consciousness only for essentially complete generalized suppression (<10 μV) after the first day of the arrest. Several other generalized patterns, including less marked suppression, burst-suppression, epileptiform activity, periodic complexes, and α-θ coma patterns, usually but not invariably indicate a poor outcome. Serial EEGs, continuous raw and automated “trending,” testing of reactivity, and the inclusion of multiple variables hold promise for an improved role in the prognostic determination in these patients. Key Words: EEG—Coma—Prognosis—Anoxic-ischemic encephalopathy.

The EEG is underused in coma. Although thalamocortical function cannot be adequately assessed clinically in the comatose patient, EEG allows for an immediate examination of cortical or cortical–subcortical dysfunction in an inexpensive, safe, and readily available manner in the intensive care unit. Although patients may show the same clinical features, especially when brainstem functions are clinically intact, the EEG can reveal a wide spectrum of abnormalities. EEG is especially sensitive to the graded severity of brain dysfunction and the direction of the process if serial tracings or continuous recordings are used (Chiappa and Ropper, 1984). Although rarely specific for the etiology of coma, the EEG may help determine the class or general category of disease process (e.g., the differentiation of seizures from metabolic or drug-induced coma). When the etiology of the coma is known, the EEG can be very useful in determining the prognosis in some conditions, especially when combined with the neurologic examination (Sharbrough, 1981). The EEG is usually dynamic: If variation does not occur within a given recording, it usually will over time. The variety and complexity of possible rhythms is inversely related to the severity of the dysfunction (Rumpl, 1987). Absolutely invariant EEGs usually indicate a severe encephalopathy and often a poor prognosis (Cant and Shaw, 1984; Karnaze et al., 1982).

The clinical importance of various EEG patterns in coma must take into consideration the clinical picture, age, etiology, acuity, and the integrity of brainstem reflexes. Most EEG patterns are nonspecific, but some findings lead to productive intervention (Jordan, 1993). EEG allows for the recognition and monitoring of treatment of seizures. In patients with vasospasm, the EEG can be used to note the response to adjustment of perfusion pressure. Certain “metabolic patterns” (e.g., triphasic waves or intermittent rhythmic δ-waves with an...
abnormal background) may trigger searches for systemic disorders or exogenous toxins. Lateralized abnormalities prompt a scan to detect a treatable structural lesion (Jordan, 1993).

It is valuable to assess reactivity or EEG change after sensory stimulation in states of decreased consciousness (Fishgold and Mathis, 1959). In general, reactivity is a feature of lighter stages of coma, but it is inconsistently associated with clinical arousability. Reactivity may exist in a variety of forms: an increase in amplitude, frequency, or even slowing (often as bisynchronous rhythmic δ-activity), or a decrease in amplitude of background rhythms. In general, EEG responsiveness is associated with a greater chance of recovery than the lack of reactivity (Fishgold and Mathis, 1959; Young et al., 1999). Reactivity should be tested in all comatose patients, unless contraindicated because of concerns regarding raised intracranial pressure. We usually test for auditory reactivity by clapping or shouting in the patient’s ears. Somatosensory stimulation should be tested by applying pressure to the nail bed of each hand and to the patient’s ears. Somatosensory stimulation should be tested by applying pressure to the nail bed of each hand and to the supraorbital nerve above the medial third of the eyebrow. Passive eye opening is recommended in suspected α-coma (no change in α) as well as a stimulus for reactivity. Because some patients may respond to only one of these stimuli, all should be tried.

There are several scoring systems for grading the severity of EEG abnormalities: for anoxic, see Hockaday et al. (1965); traumatic, Rae–Grant et al. (1991); or both anoxic and traumatic, Hughes et al. (1976), Synes (1988), and Young et al. (1997); septic encephalopathy, Young et al. (1990a); and Reye’s syndrome, Aoki and Lombrosa (1973). In attempting to determine a prognosis, however, it is best to relate the EEG to the entire clinical picture and to consider whether potentially reversible factors may be operative (Hansotia et al., 1981). The less ambiguous the categories, the better the inter- and intrarater reliability (Rae–Grant et al., 1991; Young et al., 1999).

Quantitative EEG, notably power spectral analysis, allows for trending over longer periods of time. This is useful in examining variability objectively, in charting the course of encephalopathies, and in detecting sudden changes such as those produced by seizures (Nuwer, 1988a, 1988b). Purely quantitative studies may miss major morphologic phenomena in EEG (e.g., triphasic waves, some seizures). Hence, the “raw EEG” should always be available along with the spectral plot or brain map.

Continuous EEG monitoring might best be applied to cases in which the patient is in coma with an unstable but potentially treatable condition. Examples include status epilepticus, recurring seizures, and conditions in which intracranial pressure is elevated or cerebral perfusion is variable (e.g., various neurosurgical conditions including post-traumatic coma, subarachnoid hemorrhage, tumor, postoperative cases, and hydrocephalus). Changes in frequency and amplitude, new focal features, or epileptiform activity have diagnostic and therapeutic implications that can influence management and outcome (Jordan, 1990, 1992). Continuous EEG monitoring is the best method of monitoring the depth of anesthesia achieved with barbiturates used in the treatment of status epilepticus, or even of monitoring the depth of sedation in other patients (Van Ness, 1990). This technology may be valuable in monitoring those with central nervous system disease who cannot be assessed clinically, especially patients on neuromuscular blocking agents.

Although this review is restricted to EEG, comprehensive neurophysiologic monitoring includes sensory evoked potentials (Chiappa and Hoch, 1993). These and, potentially, motor evoked responses, add new dimensions to the examination of integrity of the anatomic–physiologic subcortical pathways and primary sensory and motor cortices. The early components are not affected substantially by drugs or reversible metabolic abnormalities, whereas EEGs are. These techniques allow for the assessment of prognosis in a more robust way than has been possible with EEG alone (Chiappa and Hoch, 1993; Goldie et al., 1981; Rothstein et al., 1991). Any review of EEG in coma is hampered by the varied causes of coma, the concomitant use of sedative medications, the small number of patients in each study, the paucity of prospective studies, the nonuniform criteria for coma, the different EEG classification systems, and the absence of validation (insufficient survival times, lack of follow-up studies or postmortem correlation). With these caveats in mind, the EEG in several disease categories is reviewed, with emphasis on anoxic–ischemic encephalopathy.

### STRUCTURAL LESIONS

The role of the EEG as a primary diagnostic test for structural brain lesions has been greatly modified by the widespread use of computed tomography and MRI. However, focal EEG abnormalities should raise the suspicion of structural cerebral lesions. Furthermore, the EEG reveals the functional disturbance caused by the structural abnormality and thus plays a complementary role to imaging tests. Single structural lesions in the supratentorial compartment produce coma mainly by compression or displacement of the diencephalon or mid-brain tegmentum. EEG
manifestations may be diffuse by the time the patient is in coma, but one should suspect a supratentorial lesion if there is a marked and consistent asymmetry of voltage between the two hemispheres or if intermittent rhythmic \( \delta \)-activity is exclusively frontal (Harner and Naquet, 1975). Another mechanism by which supratentorial lesions may produce coma is by causing seizures. Epileptiform activity on EEG may suggest that an earlier seizure was missed clinically and that the patient is in a postictal state. Alternatively, nonconvulsive status epilepticus may be revealed.

Lesions limited to the brainstem often do not produce much EEG slowing; however, sleep potentials may be found in some cases. Often the EEG shows an \( \alpha \)-pattern coma that may be more marked posteriorly (Chase et al., 1968). Care should be taken that the patient is in coma and not in a locked-in state (Harner and Naquet, 1975).

As a corollary, posterior fossa lesions with marked EEG slowing probably also have dysfunction in the supratentorial compartment, especially the diencephalon, because of hydrocephalus (Harner and Naquet, 1975).

**CEREBROVASCULAR DISEASES**

Cerebrovascular disorders typically cause structural brain lesions. Statements in the previous section regarding structural lesions apply to cerebrovascular disease. Sometimes, however, the lesions are not single (e.g., in subarachnoid hemorrhage, multifocal vasospasm may cause multifocal \( \delta \)-waves or epileptiform activity [Van der Drift and Kok, 1972]). Watershed ischemia also shows bilateral abnormalities, but with maximal localization over the posterior temporo-occipitoparietal regions. The background is slow and often accompanied by periodic epileptiform activity (Niedermeyer, 1987). Thrombosis of the superior sagittal sinus and draining veins would be expected to produce a somewhat similar picture of bilateral arrhythmic \( \delta \)- and epileptiform activity, but may not be consistently maximal in the posterior head. Brainstem stroke may produce a normal EEG in the locked-in syndrome or \( \alpha \)-pattern coma or diffuse slow-wave frequencies with reduced reactivity in rostral brainstem tegmental lesions.

Metabolic consequences of cerebrovascular diseases (e.g., inappropriate antidiuretic hormone secretion and hyponatremia) may alter the EEG diffusely, as does hydrocephalus with coma.

**TRAUMA**

Trauma can affect the brain by a number of mechanisms either singly or in different combinations: hemorrhage into the brain substance or subarachnoid, subdural, or epidural space; ischemic infarction (e.g., from vascular injury, arterial spasm, or decreased cerebral perfusion pressure); axonal (shearing) injury in the white matter; associated metabolic derangements: hypoxemia, fluid, and electrolyte disturbances and sepsis; and symptomatic seizures. It is thus not surprising that there is a rich variety of EEG abnormalities. Their prognostic importance rests not only on their severity but also on the reversibility of the pathogenetic mechanisms responsible.

The following patterns have been described: slowing in the \( \Theta \)-range (Courjon and Scherzer, 1972); \( \delta \)-activity, including continuous focal arrhythmic, diffuse rhythmic, or arrhythmic or intermittent rhythmic patterns (Dusser et al., 1989; Stockard et al., 1975); faster frequencies (Loeb et al., 1959); epileptiform activity, including focal spikes or seizures, either clinical or electrographic (Silverman, 1963; Synek, 1988; Williams, 1941a, 1941b); synchronous periodic slow-wave bursts (Fishgold and Mathis, 1959); triphasic waves (Stockard and Bickford, 1975), focal suppression (Dow et al., 1961); other asymmetries (Courjon and Scherzer, 1972); and \( \alpha \), \( \Theta \)-, or spindle coma patterns (Chatrian et al., 1963; Rumpl et al., 1983; Synek and Synek, 1984; Westmoreland et al., 1975).

The timing of the EEG in head injury is very important with respect to the types of abnormalities and the associated etiologic and management implications as well as the prognosis. The comprehensive reviews by Courjon and Scherzer (1972), Stockard et al. (1975), Rumpl (1987), and Rath and Klein (1991) are recommended.

Localized abnormalities at any stage should raise the possibility of structural lesions. Changes of amplitude, especially localized reduced voltage, should be considered to reflect an intracranial hematoma until proved otherwise, provided local scalp swelling over the region is excluded (Courjon and Scherzer, 1972). Focal slowing is sometimes associated with such lesions but can occur as a transient phenomenon and may not always prove to be important. This is not uncommon in children with occipital \( \delta \)-activity. Electrographic seizures usually reflect severe brain injury, are of reliable lateralizing value, but should prompt urgent brain imaging and treatment (Courjon and Scherzer, 1972).

When the recording shows continuous rhythmic activity, including sleep phenomena, the presence of variability in frequencies and amplitude is more favorable for outcome than recordings showing no variability (i.e., a monophasic picture [Bergamasco et al., 1968; Chatrian et al., 1963]). Any reactivity is associated with a better
prognosis than no reactivity (Stockard and Bickford, 1975).

Sometimes trauma affects the brain indirectly. Fat embolism to the brain and lungs is a complication of the fractures of long bones. The patient may be asymptomatic for 12 to 36 hours after the injury and then may become obtunded in association with pulmonary symptoms and tachycardia. The EEG shows the replacement of normal rhythms with diffuse polymorphic δ- and Θ-activity, accentuated over the frontal regions (Courjon and Scherzer, 1972). Trauma to the neck may cause delayed occlusion of carotid or vertebral arteries, and clinical and EEG features of stroke in these territories.

The results of serial EEGs or continuous monitoring assist in determining the prognosis and in detecting potentially treatable conditions such as seizure activity, brain herniation, hydrocephalus, and intracerebral and subdural hematomas (Rumpl et al., 1979). The latter condition should be suspected if the EEG shows increasing slow-wave activity or focal suppression, increasing generalized slow frequencies, or chronically persisting focal abnormalities along with intermittent diffuse rhythmic δ-waves (Stockard et al., 1975). Vespa and colleagues (1999) detected seizures in 22% of patients with moderate to severe brain injury using continuous EEG monitoring. Half the seizures were nonconvulsive and would not have been noted clinically. Because there is a strong association of prolonged nonconvulsive seizures with greater mortality (Vespa et al., 1999; Young et al., 1996), continuous EEG monitoring may prove to be a valuable component of intensive care unit care. Additional work to show improved outcomes (lesserened mortality and shorter intensive care unit length of stay) would provide greater justification.

These EEG findings and their timing need to be considered along with the integrity of brainstem function and clinical responsiveness in formulating a prognosis for a particular patient (Hansotia et al., 1981; Sharbrough, 1981).

**CENTRAL NERVOUS SYSTEM INFECTIONS**

Although viral meningitis should not affect the EEG, bacterial and tuberculous meningitis usually produce irregular, widespread δ-waves as the predominant abnormality. Background activity is usually better preserved in meningitis than in encephalitis (Stockard and Bickford, 1975). The improvement in EEG frequencies parallels clinical resolution (Turrell and Roseman, 1955). In patients with a good prognosis, the EEG shows rapid normalization within 6 to 9 days (Turrell and Roseman, 1955). Prolongation of EEG abnormalities beyond 2 weeks suggests a complication such as infarction from vasculitis, hydrocephalus, or subdural hygromas (the latter in young children). Marked EEG abnormalities are associated with severe neurologic sequelae (Chequer et al., 1992).

Encephalitis also usually produces δ-waves as the most predominant abnormality (Vas and Cracco, 1990). Multifocal epileptiform activity may occur, reflecting cortical gray matter disease (Gloor et al., 1968). In herpes simplex encephalitis, one or both temporal regions are the site of maximal slowing, and between the second and fourteenth day of illness these sites often demonstrate periodic, lateralized epileptiform discharges at a repetition rate of 0.5 to 2 per second (Fig. 1; Gupta and Seth, 1973; Illis and Taylor, 1972). This diagnostic feature is especially important because herpes simplex encephalitis is specifically treatable with the antiviral agent acyclovir (Skoldenberg et al., 1984).

Multifocal δ-activity is expected in acute disseminated encephalomyelitis—a postinfectious immunologically mediated syndrome that is characterized by perivenous demyelination (Gloor et al., 1968).

**STATUS EPILEPTICUS**

Nonconvulsive seizures (NCSs) are epileptic attacks without a tonic, clonic, or tonic–clonic component. The transition from a convulsive seizure or an NCS to nonconvulsive status epilepticus (NCSE) or “subtle status” is the change of a self-limited epileptic attack to a persistent or protracted epileptic state. Nonconvulsive seizures or nonconvulsive status epilepticus is not always generalized from the onset. Some patients with focally originating seizures may develop the clinical and EEG appearance of generalized epileptiform activity (Fagan and Lee, 1990.) Thus, generalized nonconvulsive status epilepticus is heterogeneous.

Nonconvulsive status epilepticus may produce stupor or coma. Although patients with complex partial seizures are more prevalent than those with absence attacks, absence status is more common than complex partial status epilepticus. Most often these occur in patients with known seizure disorders. Eyelid flutter and rhythmic myoclonus of the face or extremities may suggest absence status, but an EEG is almost always necessary for confirmation. Absence status may occur in the elderly without a previous history of seizures, and can be missed if the diagnosis is not considered or if an EEG is not performed (Ellis and Lee, 1978). The EEG usually shows bilaterally synchronous paroxysmal discharges, often in the form of generalized spikes and waves. The repetition rate in status epilepticus may be slower (e.g., two sei-
Compared with brief absence attacks (three seizures or more per second). Nonconvulsive seizures may follow generalized convulsive seizures, and account for what is often mistaken clinically for a prolonged “postictal state.” The EEG is the only reliable means of detecting this phenomenon, and it is valuable diagnostically and prognostically (DeLorenzo et al., 1998).

**METABOLIC ENCEPHALOPATHIES**

The graded EEG response to anesthetics is similar to the evolutionary changes seen with increasing severity of metabolic derangement. There is an inverse linear relationship of EEG-dominant frequency and a direct linear relationship of amplitude (resulting from slower frequencies) with anesthetic dose (Glaser, 1972–1977). Such slowing accompanies decreased unitary activity of cerebral cortical neurons (Creutzfeldt and Meisch, 1963). This linearity breaks down at high doses with the appearance of a burst-suppression pattern or epileptiform activity. The latter may occur with some agents that produce a mixture of excitation and inhibition (e.g., diethyl ether and cyclopropane; Stockard and Bickford, 1975).

With anesthetic agents and some metabolic conditions (e.g., drug overdose and septic encephalopathy), suppression is reversible. However, in some clinical conditions, such as anoxic–ischemic encephalopathy after cardiac arrest, complete suppression signifies death of neocortical neurons, and the suppression is permanent.

**FIG. 1.** The EEG was performed on the fourth day of an illness characterized by fever, headache, confusion, and recurring complex partial seizures. There is bilateral slowing with medium-voltage $\delta$-waves in the anterior head bilaterally. Periodic lateralized epileptiform discharges (PLEDs at asterisks) occur over the right anterior–midtemporal region at intervals of just more than 1 second. (Reprinted with permission from Young GB, Ropper AH, Bolton CF, eds. Coma and impaired consciousness: a clinical perspective. New York: McGraw–Hill, 1998:250.)

**FIG. 2.** $\delta$-Waves constitute the principal finding in a patient with renal failure and sepsis. Faster frequencies are better developed on the left because of an earlier infarction in the right cerebral hemisphere. The patient recovered. (Reprinted with permission from Young GB, Kreeft JH, McLachlan RS, Demelo J. EEG and clinical associations with mortality in comatose patients in a general intensive care unit. *J Clin Neurophysiol* 1999;16:354–460.)
Thus, knowledge of etiology is vital in understanding the importance of the suppression in clinical settings.

Although many destructive, infectious, and degenerative diseases, and end-stage storage diseases involving the brain are not considered to be acute metabolic encephalopathies, the EEG may show many of the features described for the "anesthetic model" (Gloor et al., 1968; Steriade et al., 1990). In most of these diseases, in which there is death or extensive loss of neocortical neurons, the EEG changes deteriorate to various degrees of suppression and there is no clinical reversibility.

The EEG shows evolutionary changes related to the depth of anesthesia and the dose of drugs (Stockard and Bickford, 1975):

1. Desynchronization or "fast activity"
2. Increase in rhythmicity and voltage, especially δ-activity (Fig. 2)
3. Mixtures of slower frequencies with the faster frequencies; increased δ-activity with deeper levels
4. Burst–suppression, with duration of suppression becoming longer with deeper levels (Fig. 3)
5. Suppression; isoelectric EEG (Fig. 4)

Many metabolic disorders follow this basic model but show some special features or departures as well. Table 1 (Young et al., 1992) lists various metabolic and toxic diseases as they relate to the anesthesia model.

**EEG IN GENERALIZED ISCHEMIC ENCEPHALOPATHY**

From experimental studies, it is clear that ischemia is the essential component in producing neuronal death in cardiac arrest. Hypoxia alone, even with arterial oxygen concentrations of less than 25 mm Hg, does not produce neuronal death (Lindenberg, 1982; Pearigen et al., 1996). Thus, the term generalized ischemic encephalopathy is more accurate pathophysiologically. The mechanisms for neuronal death include release of excitotoxic neurotransmitters, activation of N-methyl-D-aspartate receptors with calcium influx into neurons, peroxynitrile production, failure of clearance of hydrogen ions, and lactate and free radical production on reperfusion (Dawson et al., 1988, 1993; Xia et al., 1996).

The cortical N20 response to median nerve stimulation approaches the ideal prognostic test (Bassetti et al., 1996; Goldie et al., 1981; Rothstein et al., 1991; Sandroni et al., 1999).

**FIG. 3.** (A) After cardiac arrest, this patient had a burst-suppression pattern with bursts containing epileptiform discharges in addition to waves of various frequencies. He died without recovery of awareness. (B) This patient had a burst-suppression pattern with no epileptiform discharges within the bursts. Such patients may have a better prognosis than those with the pattern shown in A. (Reprinted with permission from Young GB, Kreeft JH, McLachlan RS, Demelo J. EEG and clinical associations with mortality in comatose patients in a general intensive care unit. J Clin Neurophysiol 1999;16:354–460.)

The absence of the N20 response from median nerve stimulation is specific but is not especially sensitive for a hopeless prognosis. The lack of this response shows nearly 100% specificity for an outcome no better than a permanent vegetative state, but many patients with a preserved N20 response die without recovery of consciousness. The EEG must be compared with this as a prognostic test.

From a theoretical point of view, the EEG should be a suitable test for cortical damage or integrity. The neurons that are the most sensitive to generalized ischemic damage are those of the cerebral cortex that generate postsynaptic potentials that are recorded from scalp EEG. The EEG is flat during resuscitation; this may persist for several hours after circulation is restored (Jorgensen and Holm, 1998; Pampiglioni and Harden, 1968; Prior, 1973a, 1973b). EEG rhythms in the very young (i.e., neonates and prematures) may take longer to recover.

### TABLE 1. Metabolic encephalopathies related to the anesthetic model

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Additional features</th>
<th>Reversibility of burst–suppression or suppression</th>
</tr>
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<tbody>
<tr>
<td>Drug intoxication (Haider et al., 1971)</td>
<td>Some may produce epileptiform activity; a mixture of ( \beta + \theta ) suggestive of barbiturate or benzodiazepine overdose</td>
<td>Completely reversible</td>
</tr>
<tr>
<td>Hepatic failure (Bickford and Butt, 1955; Karnaze and Bickford, 1984; Kennedy et al., 1973; Parsons-Smith et al., 1957)</td>
<td>Triphasic waves* (Fig. 5)</td>
<td>Not reversible (older literature); potentially reversible if liver function improves or with detoxification and if severe cerebral edema is prevented</td>
</tr>
<tr>
<td>Reyes syndrome (Aoki and Lombroso, 1973; Yamada et al., 1977)</td>
<td>14 and 6 positive spikes in 50% (controversial significance)</td>
<td>Probably not reversible (dependent on damage from brain swelling and/or hypoglycemia</td>
</tr>
<tr>
<td>Uremic encephalopathy (Bolton and Young, 1990)</td>
<td>Triphasic waves* in some; photic sensitivity</td>
<td>Probably reversible</td>
</tr>
<tr>
<td>Septic encephalopathy (Young et al., 1990a)</td>
<td>Triphasic waves* in some</td>
<td>Potentially reversible if patient survives multiple organ failure</td>
</tr>
<tr>
<td>Dialytic encephalopathy (Hughes and Schreeder, 1980)</td>
<td>Epileptiform activity (generalized spike and wave)</td>
<td>Not reversible in advanced cases (aluminum poisoning)</td>
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<tr>
<td>Porphyria (Dow, 1961)</td>
<td>Focal features (e.g., spikes, suppression seen occasionally, usually transient)</td>
<td>Largely reversible; EEG may be slow to improve</td>
</tr>
<tr>
<td>Hypothyroidism (Nieman, 1959)</td>
<td>May show sharp and slow wave complexes, periods of suppression in very advanced cases</td>
<td>Should resolve, except in cretinism</td>
</tr>
<tr>
<td>Wernicke’s encephalopathy (Fournet and Lanterni, 1956)</td>
<td>Low amplitude</td>
<td>EEG may improve many patients with severe amnesia and ataxia</td>
</tr>
<tr>
<td>Addison’s disease (Dreyfus–Bresac and Mises, 1953)</td>
<td>Majority are normal; others show diffuse slowing</td>
<td>Resolves, especially with corticosteroids</td>
</tr>
<tr>
<td>Hypercalcemia (Karnaze and Bickford, 1984; Moure, 1967)</td>
<td>May have triphasic waves or FIRDA</td>
<td>Rare, resolves</td>
</tr>
<tr>
<td>Hypoglycemia (Paschen et al., 1991; Regan and Brown–Mayers, 1956; Shagass and Rowseell, 1954)</td>
<td>May show epileptiform activity, periodic complexes</td>
<td>Partly reversible, but neuronal death can occur if severe</td>
</tr>
<tr>
<td>Hypothermia (Hughes, 1978; Sadove et al., 1967)</td>
<td>Temperature dependent: no change until (&lt; 30^\circ C)</td>
<td>Burst–suppression at 20 to 22°C, suppression with temperature (&lt; 18^\circ C) completely reversible</td>
</tr>
</tbody>
</table>

* Triphasic waves were originally thought to be specific for hepatic encephalopathy (Bickford and Butt, 1955). However, they can occur in a variety of metabolic encephalopathies, septic encephalopathies, and neurodegenerative conditions (Karnaze and Bickford, 1984; Sundaram and Blume, 1987). In the context of an acute alteration in alertness, however, they are highly suggestive of a metabolic encephalopathy. In our experience, hepatic or renal failure or septic encephalopathy are the most common underlying etiologies in this situation (Young et al., 1990a).

FIRDA, frontal intermittent rhythmic delta activity.

(Reprinted with permission from the American Journal of EEG Technology. Source: Young et al., 1992.)

From a theoretical point of view, the EEG should be a suitable test for cortical damage or integrity. The neurons that are the most sensitive to generalized ischemic damage are those of the cerebral cortex that generate postsynaptic potentials that are recorded from scalp EEG. The EEG is flat during resuscitation; this may persist for several hours after circulation is restored (Jorgensen and Holm, 1998; Pampiglioni and Harden, 1968; Prior, 1973a, 1973b). EEG rhythms in the very young (i.e., neonates and prematures) may take longer to recover.
than with older patients. Thus, as a general rule, it is better to wait 24 hours or more from the event until the first EEG, unless seizures are suspected.

EEGs performed after the first day of arrest may show deteriorating patterns associated with a fatal outcome. This is supported by experimental models, in which it has been shown that the phenomenon of “delayed neuronal death” may take more than 24 hours to develop (Kirino, 1982). One must be on guard that such later suppression is not related to drugs, shock, or sepsis, however.

There is general agreement that the following EEG patterns found after cardiac arrest are strongly associated with an poor neurologic outcome: generalized suppression; generalized burst–suppression; generalized periodic patterns, especially with epileptiform activity; and α- or α-θ-pattern coma (Binnie and Prior, 1994; Binnie et al., 1970; Hockaday et al., 1965; Möller et al., 1978; Pampligioni and Harden, 1968; Prior, 1973b, pp 244–254; Scollo–Lavizzari and Bassetti, 1987; Yamashita et al., 1995; Zandbergen et al., 1998; Zaret, 1985). These patterns are addressed in the following subsections.

**Generalized Suppression**

Generalized suppression is not well defined in the older EEG literature on postcardiac arrest patients. Terms such as nearly flat, no EEG at all (presumably complete or isoelectric suppression) are not sufficiently precise, and technical criteria are not given in sufficient detail to know the voltage threshold described for these terms. In some studies, suppression is combined with other patterns that are thought to indicate an unfavorable prognosis (burst–suppression or α-pattern coma). Suppression sometimes takes time to evolve. It may not be present even at 24 hours, but only by 2 or 3 days from the time of the cardiac arrest. In Prior’s (1973b) study, 43 of 43 patients (100%) with cardiac arrest with Hockaday et al.’s (1965) grade V category (incomplete or complete suppression), either initially or on subsequent EEGs, died without recovery of consciousness. The original report by Hockaday et al. (1965) contained 14 patients with cardiac or respiratory arrest, and all 14 of patients in the group V category died. We have had at least one patient with incomplete suppression—more than 10 μV but less than 20 μV—who recovered consciousness, but none with less than 10 μV recovered consciousness. There are no reports of recovery of conscious awareness in a child or an adult with an isoelectric EEG that was recorded more than 24 hours after restoration of circulation. Autopsy reports show severe cortical damage (Brierley et al., 1971). Thus, an isoelectric EEG, recorded more than 24 hours from cardiac resuscitation, and normal blood pressure are a reliable indication of an outcome no better than permanent vegetative state.

There is a caveat with respect to the suppressed EEG. Matsuo (1985) has noted that in patients with permanent vegetative state after cardiac arrest, the EEG can vary in amplitude. Some patients appear to have a desynchronized EEG that gives the appearance of electrocerebral silence, yet with polysomnography they may show higher voltage δ-activity as a fragment of slow-wave sleep, alternating with rapid eye movement sleep. There was not, however, the full development of all four stages of slow-wave sleep.

**Generalized Burst--Suppression**

Generalized burst–suppression after cardiac arrest has usually, but not invariably, been associated with an outcome of no better than persistent vegetative state. The term burst–suppression (see Fig. 3) is meant to indicate episodes of generalized attenuation in voltage with the burst containing various frequencies (International Federation of Clinical Neurophysiology, 1983). If the bursts contain only epileptiform discharges or bisynchronous short-duration complexes and are roughly periodic, the pattern could be called generalized periodic complexes, but some may still refer to the pattern as a burst–suppression pattern. Burst–suppression again has not been well defined in published studies, and in many cases burst–suppression is lumped with other patterns. A fatal outcome occurred in all 14 patients with various generalized burst–suppression patterns in the series of Brenner et al. (1975), and in all 27 children with unspecified burst–suppression in the series of Pampligioni and Harden (1968). However, occasional survivors are found, especially in those without epileptiform discharges in the bursts (Chen et al., 1996; Cloche et al., 1968). The presence or absence of simple or even fairly complex movements (e.g., tongue thrusting, grimacing) does not alter the usually unfavorable outcome (Reeves et al., 1997). Several series have found that when generalized epileptiform activity occurs within the bursts, patients rarely recover consciousness (Pampligioni, 1964; Synek, 1988; Young et al., 1999). Similarly, generalized epileptiform discharges, either as periodic, stereotyped phenomena or as a burst of discharges, as the only EEG activity on an otherwise totally suppressed background, are almost always associated with lack of recovery of awareness.

The electroencephalographer should be aware that drugs, especially midazolam and propofol, commonly used in intensive care units, may produce a burst–suppression pattern. Opiates may produce a burst–suppres-
A theoretical concern involves patients with convulsive and subtle status epilepticus after cardiac arrest. After cardiac arrest, the occurrence of generalized epileptiform activity, either as sequential spikes or as spike and wave (Fig. 6), single or generalized epileptiform discharges as part of a burst-suppression pattern, or generalized periodic or pseudoperiodic complexes (Fig. 7) has been associated with a fatal outcome without recovery of consciousness (Celesia et al., 1988; Gaches, 1971; Kuroiwa and Celesia, 1980; McCarty and Marshall, 1981; Nilsson et al., 1972; Simon and Aminoff, 1986; Wijdicks et al., 1994). This is often associated with myoclonus or eye opening accompanying the bursts of epileptiform activity (Simon and Aminoff, 1986; Young et al., 1990b). However, Mori and Tsuruta (1983) reported such a case with a favorable recovery.

There is a striking similarity of these patterns to stages 3, 4, or 5 of the sequential changes of status epilepticus from other causes, as described by Trieman et al. (1990). (Trieman’s five stages include (1) discrete seizures: epileptiform activity occurs in discrete epochs separated by postictal slow-frequency waves; (2) merging seizures: epileptiform activity persists throughout, but the discharges wax and wane in frequency and amplitude; (3) continuous seizures: spikes and spike–waves are rhythmic and relatively constant throughout the seizure; (4) continuous with flat periods: ongoing epileptiform activity is interrupted by generalized attenuation of voltage from 0.5 to 8 seconds; and (5) periodic epileptiform discharges on a flat background: high-voltage, repetitive epileptiform discharges occur regularly against a flat or suppressed background.) The mortality rate of patients with such seizures without cardiac arrest ranges from 6% to 35% (Hauser, 1983). It is important to differentiate the fatal status epilepticus that occurs after cardiac arrest from the status epilepticus of seizure disorders. If this cannot be done clinically or with EEG, other tests to confirm the nonviability of the cortex, such as somatosensory testing, sequential EEGs, or evolutionary changes from continuous EEG monitoring, may be valuable (Goldie et al., 1981).

A caveat is the occurrence of postcardiac arrest electrographic epileptiform activity without a flat background, but with continuous background rhythmic waves. Such patients recover consciousness more commonly than those with a true burst-suppression pattern with epileptiform activity, according to Synek (1988). We have had a single case without a marked deficit. In the extensive study by Jorgensen and Holm (1998), however, no patients with this pattern recovered consciousness. Thus, this pattern is usually but not invariably evidence of severe generalized ischemic damage.
After cardiac arrest, α-pattern coma consists of diffuse or frontally predominant, continuous rhythms in the α-(8–13 Hz) frequency band (Westmoreland et al., 1975). Unlike normal α-activity, α-pattern coma is not responsive to eye opening or to stimulation. There is no fundamental difference in the etiologies, clinical picture, and prognostic importance among α-, θ-, and a mixture of α-θ-patterns, and they can be combined for practical purposes (Synek and Synek, 1984, 1987; Young et al., 1994). Patients usually remain vegetative or die without recovering conscious awareness. However, again, some patients may make a satisfactory recovery. Thus, finding an α-pattern coma after cardiac arrest is not in itself definitive prognostically (Fig. 8, top), but it should be regarded as a “transitional pattern” (Jorgensen and Holm, 1998). By 6 days after arrest, the pattern usually evolves into a prognostically definitive pattern in more than 90% of patients (Young et al., 1997). Those who die without recovering consciousness develop a burst–suppression pattern without reactivity, and those who survive have more continuous rhythms and develop electrographic reactivity to stimulation (Kaplan et al., 1999; Young et al., 1996). Alternatively, somatosensory evoked potential testing may establish the prognosis sooner (Rothstein et al., 1991).

**OPTIMAL EEG USE AFTER CARDIAC ARREST**

The literature on cardiac arrest victims indicates that somatosensory evoked potentials are a better test than a single EEG recording for determining a prognosis of no better than permanent vegetative state. EEG lacks the specificity of somatosensory evoked potentials in this regard. Furthermore, EEG is hampered by reversible factors, including drugs, sepsis, and metabolic conditions, that are prevalent in the intensive care unit, whereas the N20 response is not as affected by these factors. Apart from complete EEG suppression after 24 hours from cardiac arrest, no other single EEG pattern has a 100% association with an outcome no better than permanent vegetative state. The value of single recordings, taken in isolation, is limited to various probabilities, but never to certainty of poor outcome.

The predictive value of EEG is greatly enhanced, however, if serial or continuous EEGs are performed over several days to note trends or evolution, reactivity, and variability (Holmes and Lombroso, 1993). Furthermore, if other factors—including even partial absence of cranial nerve reflexes, absence of EEG reactivity, and variability—are included, the odds ratios for mortality without recovery of consciousness are markedly increased (Young et al., 1999). More research into the prognostic value of continuous and serial EEG studies and the use of combined variables will be valuable. A carefully performed, prospective, multicenter study with sufficient numbers should provide information that will better define the optimal prognostic role of EEG, evoked potentials, and various clinical factors individually and in combination.

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