Chapter 3.1

Standards of clinical practice of EEG and EPs in comatose
and other unresponsive states

Jean-Michel Guérit* (Belgium), Catherine Fischer (France), Enrico Facco (Italy), Paolo Tinuper (Italy), Luigi Murri (Italy), Elisabeth Ronne-Engström (Sweden) and Marc Nuwer (USA)

Introduction

Electrophysiological methods such as electroencephalography and evoked potential studies (EEG and EPs) provide functional assessment of the central nervous system (CNS). As such, their scope parallels that of the clinical examination and is complementary to that of imaging techniques (CT scan, MRI), which provide structural assessment. Indeed, CNS dysfunction may occur with or without evidence of structural lesions of the corresponding structures and CNS lesions may provoke functional disturbances that are outside the domain of the electrophysiological examination. Functional assessment can be used as an adjunct to diagnose the origin of unresponsive states, as a means to predict outcome, and for monitoring purposes (Chatran et al. 1996). The interpretation of the neurophysiological results depends on the etiology of the coma and should take into account both non-pathological factors (body temperature, drugs) and primarily non-cerebral pathological factors (peripheral sensory pathologies, metabolic disturbances) that are apt to interfere with brain function.

Domain and limits of neurophysiological examinations

Table 1 summarizes the domains of the main neurophysiological techniques available in the ICU and Table 2 shows the main EEG alterations most commonly observed in the ICU. The EEG primarily reflects cortical neuronal activity modulated by both physiological and pathological diencephalic and brain-stem influences and also affected by metabolic or toxic factors. That is,

* Correspondence to: Prof. J.-M. Guérit, Cliniques Saint-Luc, Université Catholique de Louvain, Avenue Hippocrate 10, 1200 Brussels (Belgium).

1 Much information in this chapter has been taken from two recent reviews on the same topic provided by Chatran et al. (1996) and Guérit (1999).

2 The EMG and the EPs can also be used to evaluate the peripheral nervous system, but these indications will not be considered in this paper.
many abnormal EEG patterns are non-specific as they can either correspond to a primary dysfunction of the cerebral cortex or merely reflect abnormal subcortical or metabolic influences on an otherwise intact cerebral cortex. Short-latency EPs evaluate the brain-stem, the subcortical somatosensory pathways, and the primary parietal cortex (N20). Middle-latency EPs provide assessment of the temporal (middle-latency AEPs), parietal and frontal (middle-latency SEPs), and occipital (VEPs) cortex. Long-latency exogenous and endogenous EPs depend on multiple cortical generators and are under the same influences as the EEG. Thus, a complete electrophysiological examination provides information on the function of the cerebral cortex (EEG, endogenous EPs, long- and middle latency exogenous EPs) and the subcortical pathways (short-latency SEPs and BAEPs).

The main advantage of the EEG is to provide online assessment of the cerebral cortex, contrary to the EPs, which summarize the functional status of the corresponding CNS structures over the time needed for averaging. This makes the EEG a unique tool for examining rapidly changing activities (interictal transients or seizures, triphasic waves, periodic patterns, sleep cycles, cortical reactivity to stimulation). Conversely, the averaging process diminishes the EP sensitivity to environmental noise, which can sometimes completely obscure the EEG in the ICU environment. The main advantage of BAEPs and early SEPs, not shared by the EEG, is to provide straightforward brain-stem assessment. Two limitations of the EPs should be emphasized. Firstly, they only provide assessment of the brain-stem auditory and somatosensory pathways, that is, they can remain unaltered in the presence of an anterior dysfunction limited to the motor pathways. Motor EPs to magnetic transcra
tial stimulation can theoretically bypass this limitation (Facco et al. 1993), although their use is largely limited by their sensitivity to most of the sedative drugs that are currently used in the ICU. Secondly, the early EPs can only provide reliable brain-stem assessment in the absence of major sensory patholo
gies (cochlear or auditory nerve damage for BAEPs, peripheral nerve, brachial plexus or cervical cord damage for SEPs). In the presence of these pathologies, the stimulation of other nerves

**TABLE 1**

<table>
<thead>
<tr>
<th>Neurophysiological tool</th>
<th>Componentsa</th>
<th>Normal latency range (ms)</th>
<th>Corresponding central or peripheral nervous structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cognitive EPs</td>
<td>MMN</td>
<td>&lt;200</td>
<td>Cerebral cortex, brain-stem modulation</td>
</tr>
<tr>
<td></td>
<td>P300</td>
<td>&gt;300</td>
<td>Auditory cortex</td>
</tr>
<tr>
<td>Visual EPs</td>
<td>Peak I</td>
<td>&lt;60</td>
<td>Retina</td>
</tr>
<tr>
<td></td>
<td>Peak III</td>
<td>&lt;100</td>
<td>Occipital cortex</td>
</tr>
<tr>
<td></td>
<td>Peak VII</td>
<td>150–250</td>
<td>Associative cortex, brain-stem modulation</td>
</tr>
<tr>
<td></td>
<td>RAD</td>
<td>&gt;250</td>
<td>Occipital cortex, brain-stem modulation</td>
</tr>
<tr>
<td>Somatosensory EPs</td>
<td>Erb’s point</td>
<td>&lt;12</td>
<td>Peripheral nerve</td>
</tr>
<tr>
<td>Median nerve</td>
<td>N13</td>
<td>12–16</td>
<td>Spinal cord (cervical)</td>
</tr>
<tr>
<td></td>
<td>P14</td>
<td>13–18</td>
<td>Medulla</td>
</tr>
<tr>
<td></td>
<td>P14–N20</td>
<td>&lt;7</td>
<td>Brain-stem + subcortical transmission time</td>
</tr>
<tr>
<td></td>
<td>N20</td>
<td>18–25</td>
<td>Parietal cortex (area 3b)</td>
</tr>
<tr>
<td></td>
<td>P22–N30</td>
<td>28–35</td>
<td>Central and frontal cortices</td>
</tr>
<tr>
<td>Auditory EPs</td>
<td>BAEP I</td>
<td>&lt;2</td>
<td>Auditory nerve</td>
</tr>
<tr>
<td></td>
<td>BAEP II–V</td>
<td>&lt;6</td>
<td>Pons</td>
</tr>
<tr>
<td></td>
<td>Middle latency</td>
<td>&lt;90</td>
<td>Auditory cortex</td>
</tr>
<tr>
<td></td>
<td>Long latency</td>
<td>&gt;100</td>
<td>Associative cortex, brain-stem modulation</td>
</tr>
</tbody>
</table>

a MMN, mismatch negativity; RAD, rhythmic after-discharge.
in the upper or lower limbs (SEPs) or the blink-reflex assessment should be considered.

Technical requirements

All the general standards of EEG and EP practice (this volume) should be applied in the ICU. Special care should be given to the safety measures: the technician should carefully check the equipment before the examination, current leakage should be measured regularly, and the ICU sources of electrical hazard should be identified and eliminated. This paragraph will consider both the technical requirements that are specific to the ICU and some special problems that are encountered for continuous monitoring.

Technical requirements specific to the ICU

Whatever electrophysiological technique is used, care should be taken to collect a maximum of information: possible etiology, pre-morbid clinical status, cerebral imaging if any (CT scan or MRI), clinical evaluation (Glasgow Coma Scale,\(^3\) seizures, abnormal movements), body temperature, sedative drugs, metabolic disturbances, curarization,\(^4\) scalp bleeding or collections, skull defects, ICP monitoring device, cardiac pacemakers, renal dialysis apparatus. Whenever possible, each particular examination should be performed according to a fixed protocol, with the possibility to adapt it to clinical situations. If (and only if) necessary, neuromuscular blockers are administered by qualified ICU personnel. In many instances, the routine examination can be performed by a skilled technician. However, the physician’s advice is required (1) to decide which tests must be performed, (2) whenever the standard protocol cannot be applied, and (3) to analyze the results and to integrate these in the clinical context.

**EEG recording**

Three points will be considered: the need for

| TABLE 2 |
|-----------------
| **EEG FEATURES IN THE ICU** |

| 1. **Background activity** |
| 1.1 Normal alpha (occipital, reactive to eye opening) |
| 1.2. ‘Alpha coma’ (frontal, areactive) |
| 1.3. Drug-induced activities in the alpha range (fronto-central) |
| 1.4. Theta |
| 1.5. ‘Theta coma’ |
| 1.6. Beta (symmetric/asymmetric) |
| 1.7. Delta (diffuse) |
| 1.8. Delta (focal) |
| 1.9. Spindles (symmetric/asymmetric) |

| 2. **Symmetry, reactivity, variability** |
| 2.1. Asymmetry (not posterior) |
| 2.2 Posterior suppression |
| 2.3. Reactivity |
| 2.3.1. voltage reduction |
| 2.3.2. K-complexes |
| 2.3.3. prolonged bursts of delta waves |
| 2.4. Variability |

| 3. **Additional patterns (non-pathological)** |
| 3.1. K-complexes |

| 4. **Additional patterns (pathological)** |
| 4.1. Intermittent Rhythmic Delta Activity (IRDA) (frontal or occipital) |
| 4.1.1. related to stimulation |
| 4.1.2. unrelated to stimulation |
| 4.2. Triphasic waves |
| 4.3. Episodic Low-Amplitude Events (ELAE) |
| 4.4 Alternating pattern (related to Cheyne-Stoke respiration) |
| 4.5. Epileptiform activity |
| 4.5.1. generalized |
| 4.5.2. Periodic Lateralized Epileptiform Discharges (PLEDs) |
| 4.5.3. focal spikes |
| 4.6. Burst suppression |
| 4.7. Periodic spikes |
| 4.8. Low voltage pattern |
| 4.9. Electrocerebral silence |

\(m^3\) Ideally, one should replace the GCS by the Glasgow-Liège Coma Scale (GLCS), which also considers the brainstem reflexes. However, the advantage of the GCS is that it is more easily determined, contrary to the GLCS which would carry an increased risk of carelessness.

\(m^4\) Curarization should be noted for patients with a GCS of 3. Care should be taken to note the GCS before curarization when neuromuscular blockers are used for technical convenience.

\(m^a\) Adapted from Rae-Grant et al. 1991; Niedermeyer and Lopes da
polygraphic recordings, the number of channels, and the recording electrodes.

**Need for polygraphic recordings.** In addition to the EEG recording, the examination should include that of the ECG, respiration, and body and eye movements. Video-EEG recording of abnormal movements should be performed whenever possible. Polygraphic recordings serve a double aim: (1) to help increase our understanding of the patient’s condition (periodic breathing, sleep cycles, arousal patterns, abnormal movements, etc.) and determine the relationships of these clinical events to the EEG, and (2) to disentangle cerebral activities from artifacts of non-cerebral origin. Usually, the extracerebral activities cause EEG artifacts that vary from patient to patient and from derivation to derivation. Therefore, their identification is based on their largely stereotyped appearance in a given patient and on their synchronization with the activities that are picked up in extracephalic derivations.

**Number of channels.** The number of channels depends on the clinical question to be answered, the number of available amplifiers, the number of channels devoted to the recording of extracerebral artifacts, and on possible limitations due to scalp contingencies (scalp lacerations, contusions, hematomas or sutures, skull defects, surgical drains, ICP monitoring probes, intracranial catheters).

The 16 to 21 channels of the International 10–20 System should be used whenever one has to pinpoint the location of an epileptic or a slow-activity focus, or to precise the nature of some activities (K-complexes, triphasic waves, alpha-, theta-, or alpha-theta coma). A more limited number of channels (for instance, 11) is acceptable in neonates and infants and for many usual ICU indications in adults: the evaluation of the depth of coma, the diagnosis of toxic coma, the identification of a burst-suppression pattern, the diagnosis of brain death. If the total number of amplifiers is limited, it is often preferable to replace some EEG channels by non-cerebral derivations for artifact detection.

**Electrodes.** Whenever possible, recordings should be performed with surface disk electrodes applied with colloidon and filled with conducting jelly, or held by an electrode paste with both adhesive and conductive properties. The use of electrodes inserted in a cap can minimize the risk of electrode mislocation. Needle electrodes are acceptable for recordings performed with a restricted number of channels, when local scalp conditions prevent the use of surface electrodes (scalp lesions, bandages, ICP monitoring devices) and in the absence of infection and major coagulation disorders. Local scalp conditions should always be noted by the EEG technologist. Standard sterile hypodermic platinum-iridium or stainless steel electrodes also give good results for long-lasting recordings; their higher impedance at frequencies less than 1 Hz let these act as a high-pass filter (Cooper and Binnie 1995). Needle electrodes can endanger technologist from needlestick injuries or even, if they were not disposable, endanger other patients from infection.

**EP recording**

More than with the EEG, the choice of an optimal EP strategy is dictated by the clinical issue and by the common practices of each individual laboratory. Ideally, this strategy should be adapted to study both the cortical and the subcortical EPs. Intermittent EP recordings can usually be performed with needle electrodes. Three points will be emphasized: the need for an assessment of the peripheral sensory receptors, the recording of subcortical SEPs, and the problem of artifacts.

**Assessment of the peripheral receptors.** Because the integrity of the sensory receptors is a prerequisite for using EPs to assess the central sensory pathways, it is essential that peripheral sensory pathologies be ruled out before drawing conclusions from altered wave forms. This is especially true for acute anoxia, which can cause cochlear dysfunction, head trauma, which can be associated with lesions of the ears, the auditory and the optic nerves, the brachial plexus, and the cervical cord, metabolic disturbances, which can
be associated with a peripheral neuropathy, and ototoxic drug administration.

The SEP influence of a peripheral neuropathy and of a brachial plexus or a cervical cord lesion can usually be ruled out on the basis of preserved Erb’s point, cervical and lemniscal activities. The eye integrity can be assessed by the ERG; however, absent VEPs with a unilaterally or bilaterally preserved ERG do not exclude a bilateral optic nerve lesion in acute traumatic cases. In many cases, the influence of a cochlear pathology is excluded by the use of higher stimulus intensities.

The use of an ear or a non-cephalic reference for scalp median-nerve SEPs. The use of an ipsilateral ear reference for the scalp recordings of median nerve SEPs discloses the lemniscal P14 or the P13–P14 complex in addition to cortical activities (Figs. 2–5). This allows us: (1) to rule out extracranial pathologies as the origin of null cortical SEPs; (2) a better definition of the brainstem conduction time by calculation of the P14–N20 interpeak latency; (3) to make a differential diagnosis between brain death (P14 absent) and some extreme cases of vegetative states associated with a loss of cortical EPs (P14 present). The use of a non-cephalic reference allows to disclose the N18 in addition to the P13–P14 complex, the recording of which can be important to check the level of rostro-caudal deterioration. However, it exposes to a high rejection rate due to contamination by ECG artifacts.

Muscle and blink artifacts. Because the frequency spectrum of the surface EMG overlaps that of SEPs, BAEPs, and middle-latency AEPs, these can be non-recordable in poorly responsive patients in whom muscle relaxation cannot be obtained, in which case it is usually impossible to obtain superimposable recordings. In other cases, exaggerated reflexes or startle reactions introduce spurious activities of muscular origin, which are synchronized to the stimulus and can be confused with activities of cerebral origin. These artifacts can be removed by curarization in intubated patients. Blink artifacts can also introduce spurious activities particularly in VEPs and cognitive EPs; these are usually easily identified by an additional eye derivation.

Technical requirements for continuous EEG and EP monitoring

There are several pathophysiological processes to which the EEG and the EPs are sensitive: brain ischemia, increased intracranial pressure, subclinical seizures, metabolic and toxic encephalopathies. Early detection of these processes may pick up these conditions at a reversible stage, thereby preventing their life-threatening consequences. This justifies continuous neuromonitoring.

Electrodes

The long-term installation of surface electrodes can produce skin compressive lesions and irritation, especially in comatose patients. This is especially true for electrodes inserted in a firmly-attached electrocap, which should be removed at least once a day. Disk electrodes applied with collodion are likely to give the best results. These should be filled with conductive jelly at least twice a day and their impedances measured. Gathering together the electrode wires and enclosing them in a tubular stocking, wrapping the patient’s head with a wide elastic bandage through which the electrodes can be refilled, and subsequently keeping it covered with a stocking cap, are additional measures which minimize electrical interference and other artifacts. Sterile intradermal platinum-iridium needles fixed with surgical tape and a head bandage have been successfully used for up to 1 to 2 weeks by one of the authors (E.R.-E.). They present the great advantage of not giving rise to any artifact on the CT-scan, unlike surface electrodes.

Artifacts

Continuous EEG monitoring raises new artifact problems that should be dealt with by the digital EEG recorder. These artifacts may be due to electrode-paste drying up (when working with surface electrodes) or to electrode displacement by the nursing team or to the patient’s movement (especially when working with needle electrodes), to movement or muscle contamination in non-curared patients, or to the sudden appearance of envir-
omental noise. It is essential that all artifacts be identified on the trend curves, either automatically or by the nursing team. Only those artifacts such as irreducible line interference or intermittent external electrical interference comparable do diathermy in surgical procedures should be automatically removed from the trend curves, which can then take a discontinuous aspect.

**Number of EEG channels**

Because of the need to translate the EEG information into a readily interpretable message, it is usually preferable to decrease the number of EEG channels to a minimum of two, the derivations of which should be adapted to the clinical problem to be dealt with, usually by reference to a preliminary multi-channel recording. The interpretative limitations caused by this lower number of channels should be clearly explained to the intensivist and repeat conventional EEGs undertaken regularly to check that those selected for continuous monitoring remain valid.

**Additional requirements for continuous EP monitoring**

The application of continuous sensory stimulations would be contrary to the requirements of brain protection protocols, which aim to maintain cerebral metabolic activity at the lowest possible level consistent with neuronal viability. Therefore, the EP recordings should be carefully scheduled and adapted to the clinical situation.

**Which neurophysiological parameters should be monitored?**

Continuous neuromonitoring constitutes a neurophysiological tool to be used by non-neurophysiologists. In other words, the interpretation of neurophysiological data is usually outside the training or experience of surgeons, intensivists or anesthesiologists, for whom this information is so crucial for proper clinical management. That is why the neurophysiological information must be coded into a language that is readily interpretable by the user.

A 3-step procedure can help solve this problem. The first step consists of a quality screening followed by an automatic neurophysiological feature extraction. It relies on the frequency analysis of steady EEG segments, the time analysis of transients, and the automatic identification of EP peaks. The second step consists in selecting and recombinig these parameters in order to define neurophysiological patterns which better characterize the process to be monitored. This test can be performed at a more or less elaborated level. At the most elementary level, the Fourier parameters can be recombined to provide the classical parameters of spectral analyses (absolute or relative powers, median frequencies, spectral edges, etc.) and user-defined indexes (asymmetry index, power ratios, etc.). Time analyses can provide identification of specific patterns such as burst suppression, complex arousal patterns and epileptiform discharge, EP and EEG encephalopathy grades, and electrocerebral inactivity. At a more highly elaborated level, different neurophysiological tools can be recombined to reflect the patient’s overall CNS function. For example, the combination of BAEPs and SEPs can be used to differentiate pontine from midbrain involvement, thereby providing a unique tool for early detection of the brain-stem involvement in transtentorial herniation. The third step consists of the integration of neurophysiological features into the clinical context, often by reference to evidenced-based data libraries showing clusters or patterns of high specificity and sensitivity.

**Training of intensivists and the nursing team**

Because the neurophysiologist cannot be present throughout the entire period of neuromonitoring, it is essential that intensivists and the nursing team be trained in some basic principles of EEG interpretation and the way to react to the most commonly encountered technical problems. A trained neurophysiologist and an EEG technologist should be reachable for the remaining problems.

Besides this, recordings in the ICU require neurophysiologists and technicians properly trained in the prevention of transmitted infections and in taking precautions against electrical hazards (Cooper and Binnie 1995). Local, national, and
international rules and regulations should be regularly checked.

The importance of the etiology of coma

The sensitivity of any electrophysiological technique depends on its ability to evaluate the CNS structures that are the most sensitive to the pathophysiological process at the origin of coma, which, in turn, depends on the coma etiology.

In anoxic coma, several factors determine the sensitivity of a given brain region to global brain hypoperfusion: its basal metabolic rate (the higher the metabolism, the more sensitive the structure), its situation with respect to the major intracranial vessels (the watershed zones are the most sensitive when an ischemic component is present), and arteriolar tone (the capacity for autoregulation of cerebral blood flow may be pathologically or pharmacologically impaired). The former factor explains why, for a given brain region, the grey matter is always more sensitive than the white matter, and why, for a given histological structure, the cerebral hemispheres are always more sensitive than the brain-stem. The second factor explains the elective sensitivity of the medio-frontal and parieto-occipital cortex. Consequently, the EEG, the endogenous EPs, and the cortical components of exogenous EPs are the most sensitive techniques, while the BAEPs and the early SEPs are more resistant.

The pathophysiology of traumatic coma is more complex. Indeed, 3 main factors determine both the current clinical status and the patient outcome: the presence and the location of focal brain lesions (supratentorial contusions or primary brain-stem lesions), the extent of diffuse axonal injuries in the cerebral hemispheres, and the immediate and long-term consequences of an increased intracranial pressure. Even if supratentorial contusions may give rise to focal EEG slowing or asymmetries of cortical EPs, these are more easily diagnosed with imaging techniques, which are usually available in the ICU. Diffuse EEG slowing combined with diffuse cortical EP abnormalities indicate the existence of a widespread cortical dysfunction, which can be the consequence of diffuse brain edema and increased intracranial pressure, diffuse axonal injuries but sometimes merely reflects the influence of midbrain lesions. Unfortunately, they do not differentiate these situations; the BAEPs, middle-latency AEPs, and early SEPs constitute valuable adjuncts as they can indicate the presence of either midbrain (in case of primary midbrain lesion) or combined midbrain and pontine (in case of transtentorial herniation) dysfunction (Fischer et al. 1994).

The influence of non-neurological factors

The EEG and the EPs recorded in the ICU are the outcome of a complex mixture of factors including: (1) the primary neurological factors due to the pathophysiological process under study, (2) non-neurological factors interfering with cortical or brain-stem activity. Thus, for a given degree of EEG or EP alteration, the influence of the primary neurological factors is likely to be all the lower as non-neurological factors are present at the same time. The non-neurological factors that are apt to influence the EEG and the EPs include body temperature, metabolic disturbances, the effects of neurotropic drugs, and various sensory factors.

Body temperature

At the body temperatures usually present in the ICU, hypothermia causes EEG slowing, an increase in the SEP central conduction time (in the order of 0.6 ms/deg for the P14–N20 IPL) and in all BAEP interpeak latencies (in the order of 0.2 ms/deg for the I–V IPL). The EEG disappears at a mean temperature of 24°C. In the SEPs, N20 and P14 disappear at mean nasopharyngeal temperatures of 21°C and 17°C, respectively (Guérin 1998). BAEPs disappear at 20°C. That is, the EEG never becomes isoelectric and the intracranial EPs never disappear in the temperature ranges usually encountered in the ICU. Hyperthermia can also reversibly silence the EEG (Cabral et al. 1977)

Metabolic disturbances

Hepatic encephalopathy. Hepatic encephalopathy is associated with: (1) a progressive slowing of the EEG; (2) an initial increase, followed by a
decrease, in EEG amplitude, a discontinuous pattern, and an isoelectric EEG; (3) the appearance of triphasic waves. Stupor is often, but not always, associated with triphasic waves. Coma usually is associated with delta waves (Daly and Pedley 1990). The following grades were defined in adults on the basis of the EEG frequency: 7–8 Hz (Grade 1), 5–7 Hz (Grade 2), 3–5 Hz (Grade 3), <3 Hz (Grade 4). Grade 4 has been subdivided into Grade 4a (continuous EEG) and Grade 4b (discontinuous EEG).

The EEG changes are associated with alterations of the cortical EPs. The subcortical EPs seem to be more resistant as, for instance, acute hepatic failure does not give rise to BAEP and early SEP changes, even in the presence of a Grade 4 EEG. If the subcortical conductions are abnormal, one has first to rule out a preexisting or an associated brain-stem lesion (chronic alcoholism, central pontine myelinolysis), an associated uremic encephalopathy, or the influence of drugs (see below).

_Uremic encephalopathy._ Besides an EEG slowing similar to that observed in hepatic encephalopathy, kidney failure more often causes spiking, with or without clinical concomitants.

Although the changes in cortical EPs are similar to those observed in hepatic encephalopathy, acute renal failure is usually associated with a slowing of brain-stem conduction.

**Clinical relationships.** As a rule, the EEG changes consecutive to the metabolic encephalopathies parallel the mental alterations more closely than the metabolic changes. Moreover, the EEG and cortical EP alterations that are observed in metabolic disturbances usually correspond to the reaction of a normal brain to an abnormal metabolic environment. That is, the importance of the EEG or cortical EP alterations usually reflect the intensity of the underlying extracerebral problem, rather than a primary, prognostically relevant, brain dysfunction. For example, an markedly abnormal EEG associated with major hepatic failure can recover immediately after liver transplantation (Fig. 1). By contrast, there are no instances in which BAEP loss or the disappearance of the SEP N20 were explained exclusively by metabolic disturbances. That is, such observations imply the existence of an additional brain pathology, usually with an ominous prognosis.

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![EEG Tracing](image)

**Fig. 1.** EEG in hepatic encephalopathy. Comparison of recordings performed before (March 4, 8 p.m.) and after (March 5, 7 p.m.) orthoptic liver transplantation (OLT). Note the rapid EEG recovery after OLT (courtesy of Paolo Tinuper, University of Bologna).
Drug EEG influences

Most anaesthetic or major sedatives agents, including halogenated gases, thiopental, midazolam, etomidate, and propofol, cause similar EEG changes: first the disappearance of the alpha rhythm and appearance of beta activities, and then a progressive slowing toward theta and delta rhythms. Deep anesthesia or heavy sedation with barbiturate or benzodiazepine agents in particular, are associated with a burst-suppression pattern. At the deepest level of anesthesia (but more rarely with ICU sedation regimes), the EEG may disappear. Ketamine differs from these agents in that the alpha disappearance is followed by rhythmic theta activities before delta waves appear. Thus, it appears that, although the anaesthetic agents may somewhat differ at low doses, all share the common features at higher doses of causing EEG slowing followed by burst suppression and, eventually, an isoelectric pattern. When used at high doses, opioid agents like sufentanil or alfentanil usually do not give rise to beta activities but cause immediate EEG slowing with high voltage, slow delta waves. The EEG is not altered by curarization per se.

EP influences. The EP influences of most anesthetic agents can be forecast on the basis of two simple rules (Guérith 1998). First, all lipophilic agents interfering with neuron membranes (halogenated gasses, propofol, thiopental) also interfere with subcortical conduction and so cause an increase in both the BAEP interpeak latencies and the SEP central conduction time; by contrast, there is no reason for subcortical conduction to be influenced by agents that only interfere with brain receptors (opioids, benzodiazepines). Second, all agents interfering with the EEG also interfere with the EP components belonging to the same frequency range as the EEG either through direct action on cortical generators or through variations in the signal-to-noise ratio due to a high EEG amplitude or to the occurrence of the burst-suppression pattern.

Sensory pathologies

Although the sensory pathologies per se do not influence the EEG in the ICU, the possibility of a major sensory deficit should be taken into account whenever the EEG reactivity is tested (for example, the EEG can be reactive to pain stimulation, but not to auditory stimuli in case of a bilateral petrous bone fracture; the reverse picture can be observed after a spinal cord transection). Moreover, a busy ICU may give continuous acoustic stimulation, which can cause several forms of EEG reactivity, like prolonged bursts of delta activity, EEG voltage reduction, or the appearance of rhythms in the theta or, more seldom, alpha frequency range. The presence of unrecognized acoustic stimuli should always be suspected, especially when identical transient changes are observed when specifically testing the EEG reactivity.

Clinical applications

Intermittent EEG and EP recordings

Diagnosis. Both the EEG and the EPs lack etiologic specificity and the neuroimaging techniques (CT scan, MRI) allow a straightforward diagnosis of most cortical and brain-stem lesions. Therefore, diagnosis is usually not the primary aim of the neurophysiological examination. There are some exceptions: the detection of epileptiform discharges or repetitive complexes specific to certain encephalitides, the differentiation between toxic/metabolic factors and structural lesions in comas of unknown etiology, support for the diagnosis of brain death, and the diagnosis of de-fferented states or of psychogenic unresponsiveness.

The diagnosis of abnormal movements that might be epileptic seizures and of non-convulsive (subclinical) status epilepticus. The EEG can confirm the presence of generalized or focal seizures following head trauma even when muscle relaxants or major sedatives modify their clinical expression. Indeed, the diagnosis of non-convulsive seizures forms a useful application of the EEG in ICU. Conversely, the EEG can help to rule out epilepsy in the presence of various movements that resemble epileptic activity but that are not, in fact, epileptiform: these include infection-related rigors, tetanic spasms, myoclonic
jerks, ischemic tremors, neuroleptic malignant syndrome, medication-induced extrapyramidal movements, tonic head or eye deviations, and decerebrate or decorticate posturing (Jordan 1995). This latter, as part of an abnormal arousal response, is quite commonly misdiagnosed and can be differentiated from seizures by observing the relationship of clinical and EEG features to the most common provocative stimuli, e.g. voices or noise at the bedside, nursing procedures such as oro-pharyngeal suction etc.

The differentiation between toxic-metabolic factors and structural lesions. Two characteristics of the EEG strongly favor the metabolic/toxic hypothesis: the presence of triphasic waves, which suggests a metabolic encephalopathy, and the predominance of beta rhythms, which suggests a toxic coma. For the EPs, the finding of an isolated latency prolongation in the absence of wave-form distortions strongly favors a mere dysfunction of otherwise intact sensory pathways. Conversely, the presence of focal EEG alterations or BAEP and/or early SEP wave-form distortion or asymmetry strongly favors the hypothesis of structural lesions. Because the CT scan may not be sensitive enough to discrete brain-stem lesions and MRI availability is limited in many ICUs, the EPs sometimes constitute a unique tool to diagnose infratentorial lesions.

The diagnosis of brain death. The diagnosis of BD is basically clinical (areactive coma, loss of brain-stem reflexes, apnea). The origin of coma must be known as sufficient as to cause BD. Electrophysiological testing should only be considered as a BD confirmatory tool. BD corresponds to the destruction of the whole encephalon and is therefore associated with an isoelectric EEG and with the loss of all the EPs of intracranial origin (including the BAEP peaks II–V and the P14–N18 in median-nerve SEPs) contrasting with the preservation of all the activities of extracranial origin (sensory nerve action potential, electroretinogram) and with a variable preservation of the BAEP peak I (Figs. 2 and 5). The specific requirements for EEG recording in suspected BD can be found in Table 3.

Even if the EEG has long been considered the classical neurophysiological tool to confirm BD, it actually presents 3 major problems: (1) its recording must be performed at maximal amplification, which gives rise to contamination by environmental noise and, sometimes, to ambiguous results (Fischer 1997); (2) the EEG can be isoelectric in reversible circumstances: CNS depressant drugs,

![Fig. 2. EP pattern of brain death (BD). Flash VEPs (top left) are restricted to peak I, which is synchronized to the ‘b’ component of the ERG. The comparison of recordings performed between $C_1$ and the outer canthus of the left (OC1) and the right (OC2) eyes shows that right eye stimulation gives rise to activities only in the ipsilateral channel, thereby excluding the participation of $C_2$. BAEPs (top right) are null after stimulation of the left ear and restricted to an ill-defined peak I after stimulation of the right ear. Median nerve SEPs disclose a well-preserved sensory nerve action potential and cervical activities (bottom left), but only P13 appears in the scalp to linked-ear (LE) recordings (bottom right). The P13 appears as a monophasic wave and its latency, contrary to that of P14, never exceeds the N13 latency by more than 0.8 ms at body temperatures higher than 35°C.](image-url)
deep hypothermia, profound hypotension, severe metabolic or endocrine disturbances, encephalitis; (3) the EEG does not assess the brain-stem, whose destruction should be proven to establish BD. The conditions mentioned in (2) should be ruled out before using the EEG as a confirmatory tool of BD. Other, probably more reliable, confirmatory tools are the short-latency multimodality EPs, which directly evaluate the brain-stem, and the direct measurement of cerebral blood flow by angiographic or radioisotopic techniques. Transcranial Doppler appears to be another valuable tool (Ducrocq et al. 1998).

The diagnosis of the de-efferented states and psychogenic unresponsiveness. In the absence of other interfering factors, the EEG and the EPs are normal in psychogenic unresponsiveness. The EEG can sometimes be of low voltage, in which case the EEG reactivity should be cautiously tested. In the de-efferented states, the EEG still exhibits a posterior reactive alpha rhythm and the VEPs are normal. The BAEPs and the early SEPs are variable: these can be normal when the lesion is restricted to the motor pathways but can be strongly altered if the lesion spreads towards the auditory or somatosensory afferent pathways. The P300 can help to confirm the de-efferented state; however, the auditory P300 can be absent in the presence of a brain-stem lesion interfering with the auditory pathways, in which case it may be necessary to record visual P300s.

Prognosis

General principles. For any test, the prediction of clinical outcome depends on the test’s sensitivity and specificity and can be evaluated in terms of negative and positive predictive value. As a rule of thumb, a test that is more sensitive to the pathological process determining prognosis has a higher predictive value for a good prognosis if negative but a lower predictive value for a poor prognosis if positive. Conversely, a test that is more resistant has a lower predictive value for a good prognosis if negative and a higher predictive value for a poor prognosis if positive. Moreover, the test specificity is inversely related to its dependence on prognostically-unrelated factors: the more specific the test, the better its positive predictive value.

Another issue is to establish whether the predictive value of the EEG or the EPs is really superior to that of the clinical examination. The insensitivity of both techniques to neuromuscular blockers explains their great value in curarized patients who cannot be clinically evaluated.

Prognosis in anoxic coma. The value of the EEG to predict outcome in anoxic can be considerable providing the patient does not have high levels of CNS depressant drugs either from self-poisoning or from sedative regimes. In general terms, a mildly altered and reactive EEG is usually associated with a better prognosis, irrespective of whether sedative drugs are used or not. Conversely, in the absence of sedatives, a burst-suppression pattern that persists through the first few hours is associated with an ominous prognosis.

The prognostic value of the EPs depends on which activities are considered. Cognitive and long-latency EPs are very sensitive to brain anoxia but are subject to the same drug influences as the EEG. Therefore, their presence is usually associated with a good prognosis but their absence does not allow any conclusion to be drawn. Conversely, short-latency EPs are resistant to anoxia. Therefore, no conclusion can be drawn from the presence of the N20 in early SEPs, but its bilateral absence more than 24 h after the onset of anoxic coma has been uniformly associated with death or the vegetative state (Fig. 3). Zandbergen et al. (1998) recently concluded from a meta-analysis study that the SEP recording was the most useful method to predict poor outcome in anoxic-ischemic coma.

The SEPs can usefully complement the EEG in the presence of an alpha, theta, or alpha-theta coma. Indeed, the alpha coma is usually associated with an ominous prognosis in the absence of sedative drugs but can be associated with recovery in 10% to 20% of cases. The alpha coma is always associated with a bilateral loss of N20 in patients who did not recover and with the preservation of N20 in patients with a favorable outcome.

The BAEPs are not a good tool to predict
outcome in brain anoxia. They are usually normal. They can be absent shortly after the onset of coma, owing to post-anoxic cochlear dysfunction, and reappear within 24 h. BAEPs are very rarely compatible with a pontine lesion, in which case the possibility that cardiac arrest was actually due to a primary infratentorial pathology should be considered.

**Prognosis in head trauma.** Head trauma differs from brain anoxia in that both the cerebral hemispheres and the brain-stem can be involved. Many patients with severe head injury are managed with sedative drug regimes. That means that the EEG often has limitations for use in predicting outcome. Two indicators of a good prognosis seem to be the presence of an EEG reactivity and the recognition of sleep related activities in the polygraphic recordings. Rae-Grant et al. (1991) proposed an EEG rating scale using dichotomous variables including the background activity, the symmetry, reactivity, and variability of the EEG, and additional patterns like epileptiform activities, burst suppression, low voltage, and electrocerebral inactivity. A significant relationship was found between their system and the Glasgow Outcome Scale, although there remained some overlap between the EEG scores of patients with a poor or a good outcome.

Numerous studies deal with the EP alterations in head trauma, which can be clustered into four main patterns (Guérin et al. 1993). Pattern 1 is similar to that seen in brain anoxia and consists in alterations of cortical EPs without abnormalities of the BAEPs or SEP brain-stem conduction time. It usually predicts a good outcome. Pattern 2 corresponds to midbrain dysfunction (normal BAEPs contrasting with abnormal middle-latency AEPs, abnormalities of the SEP central conduction time) (Fig. 4). Its prognostic value depends on the degree of VEP and SEP alterations. Pattern 3 corresponds to trans-tentorial herniation (Fig. 5). It is usually associated with absent cortical EPs and rostro-caudal deterioration of the BAEPs and is uniformly associated with death. Pattern 4 corresponds to BD. This classification is in keeping with previous ones, which had demonstrated the good negative predictive value of long-latency EPs and the more variable prognosis associated with primary brain-stem pathologies.

**The importance of the time elapsed from the acute episode.** The prognostic value of both the EEG

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**Fig. 3.** EPs in anoxic coma (60-year-old male resuscitated from circulatory arrest, GCS = 3, EEG: burst-suppression pattern). (A) There are no reproducible cortical VEP components but the ERG is preserved. (B) Median nerve SEP disclose well-structured cervical components, scalp to linked-ear (LE) recordings only exhibit a P14 whose latency (15.9 ms) exceeds by 2.1 ms that of the cervical N13 (13.8 ms). After left median nerve stimulation, P14 is followed by a broad negativity likely to correspond to N18. Digital subtraction of the LE-Fp1 from the LE-C' shows channel only discloses an ill-defined upward deflection synchronous to P14 (due to the fact that P14 amplitude is always higher at Fp1 than at C'3), but no subsequent cortical components. This subtraction confirms that scalp-to-scalp recordings (Fp1-C'3) are associated with an almost total P14 cancellation. (C) BAEPs are normal. This pattern, which carries an ominous prognosis, should be compared with the BD pattern (Fig. 2) in which P14 is absent and BAEPs are null or restricted to peak I.
value of mild alterations diminishes in patients who are still comatose more than 7 to 10 days after the acute episode. This finding can be explained by the fact that both reversible neuronal sideration and irreversible structural lesions account for the neurophysiological abnormalities and the EPs depends on the time elapsed from the acute episode, especially in anoxic coma. As a rule of thumb, important alterations should be more cautiously interpreted within the first 24 h after the acute episode, while the negative prognostic

Fig. 4. Pattern 2: Midbrain dysfunction (confirmed by MRI) after head trauma (19-year-old male, GCS = 4, normothermic, EEG: aspecific diffuse slowing). (A) The VEPs show well-preserved, though delayed, occipital components. (B) Left median nerve SEPs disclose intact cervical components and P14 but no cortical components. Right median nerve SEPs show a preserved N20 but an increased central conduction time (9 ms). (C) BAEPs: Peak I is absent after right ear stimulation. Left-ear stimulation shows a well-structured, but delayed peak 1 without abnormalities of the I-V interval. This pattern is compatible with normal cervical, medullar (intact P14) and pontine (intact BAEPs to left-ear stimulation) conduction and relatively preserved cortical activities (VEPs, EEG). The SEP abnormalities can be explained by a right predominant midbrain dysfunction. This patient regained an independent life with well-preserved cognitive functions and a mild left hemiparesis.

Fig. 5. Head trauma. Evolution from Pattern 3 (transtentorial herniation) to Pattern 4 (brain death). Comparison of two examinations performed at 10 a.m. (areactive coma, loss of corneal and pupillary reflexes, preserved oculo-vestibular and oculo-cardiac reflexes) and 4 p.m. (clinical pattern of BD). Flash VEPs (top left) were restricted to peak I since the first examination. Note the synchronization of peak I with the ‘b’ wave of the ERG. The BAEPs (top right) performed at 10 a.m. only disclose peak I after left ear stimulation and peaks I to IV after right ear stimulation. At 4 p.m., BAEPs are null after left ear stimulation and restricted to peak I after right ear stimulation. At 10 a.m., median nerve SEPs (bottom curves) show preserved sensory nerve action potential, cervical components, and P14. At 4 p.m., the sensory nerve action potential and the cervical N13 are still present P14 has disappeared and is replaced by P13 (note the small negative latency shift and the marked amplitude decrease of the positivity). The Erb’s point and cervical recordings (bottom right) were performed with a Fpz reference, giving rise to their initial contamination by P14, which has disappeared in the control examination performed at 4 p.m.
that are observed at the acute stage of coma, while only irreversible structural alterations can explain equivalent EEG or EP alterations that are observed later on.

Continuous EEG and EP neuromonitoring
Continuous neuromonitoring is indicated for all pathophysiological processes whose early detection is required to prevent long-lasting consequences. Neuromonitoring is a bedside technique, whose specificity resides in its ability to mark the time when possibly harmful complications are occurring and to orientate the patient toward other techniques for more precise anatomical or pathophysiological investigations. In a series of 200 consecutively monitored patients, Jordan (1995) found that the impact of ICU continuous EEG on clinical management was decisive in 54% of cases, contributing in 32% and null in 14%.

Early detection of evolving events
The monitoring of ischemia. One particularly interesting feature of the EEG and the EPs is their ability to detect the ischemic penumbra, that is, the pathophysiological state occurring in acute ischemia in which neurons are non-functional but still alive and salvageable by reperfusion. As neuronal dysfunction can be immediately detected by EEG or EPs, there is time to reverse the process and prevent irreversible structural damage. Which technique is best suited to detect the ischemic penumbra actually depends on the clinical situation.

Guériot (1998) summarized the interest of EEG and EP monitoring for early detection of brain and spinal cord ischemia.

The detection of non-convulsive seizures. The incidence of non-convulsive seizures in ICU patients has been found the highest in brain tumors (54%), uncontrolled seizures (56%) and metabolic comas (60%); these were also described in intracranial infection (33%), head trauma (28%), acute cerebral ischemia (26%) and intracranial hemorrhage (22%) (Jordan 1995). There is widespread agreement that they should be detected and treated as (1) these patients have a higher probability of developing convulsive seizures, and (2) they can diminish the patient’s alertness and prolong the ICU stay. Because they occur only every several hours in some patients, they can remain undetected by routine EEG testing.

The neurological consequences of increased intracranial pressure (ICP). In conjunction with ICP monitoring devices, neuromonitoring can help detect the brain-stem consequences of increased intracranial pressure. Pfurtscheller et al. (1987) designed a system for continuous monitoring of EEG spectra and brain-stem and somatosensory EPs that is particularly suited for this indication.

Follow-up of hepatic encephalopathy. An aggravation of the degree of encephalopathy
constitutes one of Child’s criteria for liver transplantation in patients with acute hepatic failure.

Long-term forewarning of the neurological complication of subarachnoid hemorrhage and increased intracranial pressure

Evidence gained from intracerebral microdialysis in patients with severe head injury and subarachnoid hemorrhage shows that alterations of brain metabolism can precede neurological complications by hours or days. This raises interesting perspectives for early forewarning of vasospasm or increased intracranial pressure. Although the second indication is still matter of perspective, the former has already been introduced into ICU practice. Indeed, Vespa et al. (1997) described a loss of EEG variability as a forewarning sign occurring 0 to 2 days prior to the occurrence of vasospasm in patients with subarachnoid hemorrhage.

References


