

12 ELECTRICAL FUNCTION MONITORING

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12.1 Goals

The goals of electrophysiological monitoring are to provide a continuous, objective and readily interpretable measure of brain function in the comatose head-injured patient. As with any monitoring system, one would like to detect potentially serious complications and intervene before they result in permanent morbidity or mortality. Information about the localization of focal lesions would also be helpful, although this has decreased in importance since the advent of modern radiological imaging studies (i.e. computed tomographic scanning and magnetic resonance imaging). Another potential use of electrical function monitoring is the measurement of the therapeutic efficacy of new drugs or other therapies for head injury. Ideally one would be able to determine in the acute phase whether the agent was exerting the hoped-for beneficial effects, obviating the requirement of waiting weeks or months for the standard clinical outcome measures. Eventually one might be able to titrate therapy based on real-time neurophysiological response, in a similar way as is currently done in respiratory and cardiovascular intensive care.

The monitored parameter or function should ideally have low variability, so that a change over some period of time indicates some real change in cerebral function rather than normal random physiological variability, yet should be sensitive enough to detect change sufficiently early to allow treatment to be rendered in a timely fashion. The monitored function should also be relatively resistant to the effects of typical sedative and analgesic drugs, used in customary dosages. As will be seen, the sensitivity of monitored responses to sedative and analgesic medications varies widely among electrophysiological measures. The interpretability and ease of use of the measured parameter is a function of the volume and complexity of information generated. A monitoring technique that yields an overwhelming amount of information will not be practical to use; nor will one

that produces information that is only meaningful to experts trained in electrophysiology. To be clinically useful in a monitoring application, the information must be easily interpretable by nurses and non-expert medical personnel. These issues have started to be addressed within the last few years.

12.2 Problems and limitations

Problems with electrophysiological monitoring may be broadly classified into three areas:

- technical issues surrounding the recording of the signal (most frequently corruption of signal by noise);
- problems with data display and interpretation specific to the method of monitoring (alluded to above);
- most fundamentally, the fidelity with which the monitored parameter reflects the pathophysiology of the disease of interest.

Clearly, monitoring a parameter that changes significantly only in the end stages of a disease process is likely to yield little or no benefit in terms of early detection and prevention of morbidity. Measurements that are overly sensitive to normal physiological variation may disguise significant events or trends within this normal variation until it is too late to act on the evolving trend (the 'forest and trees' problem). Brain-stem auditory evoked potentials (BAEPs) offer an example of the former, whereas the variability and extreme sensitivity of the electroencephalogram (EEG) and its processed derivatives to drug effects cause problems of the latter type (see below).

Technical issues that have been problematic in the past, such as the size of electrophysiological monitoring apparatus and contamination of signal with noise, continue to shrink in relative importance with the improvement in electronic components and the advent of computerization of monitoring equipment. Monitoring systems have been made smaller and

portable and now can be brought to the bedside with relative ease. Improvements in analog and digital signal filtering have made recording good-quality signal possible in previously electrically hostile environments such as intensive care units. Recording in special electrically shielded rooms is no longer essential. Computer control of recording systems makes the unattended operation of these systems possible, obviating the need for (and excessive cost associated with) full-time attendance of a technician at the bedside. Computerized display systems, digital storage of data, computerized feature extraction and data reduction techniques are beginning to shrink the enormous amount of data associated with continuous or very frequent data recording, and to simplify its interpretation by non-experts. Having surmounted many of the technical obstacles to electrical function monitoring, it now remains to answer the more fundamental questions about how faithfully these methods monitor the progress or deterioration of patients with severe head injury and what are the optimal electrophysiological parameters to monitor. The balance of this chapter will be devoted to these questions, as well as providing the reader with an introduction to the technical principles concerning the recording and physiological origins of these signals.

12.3 Methods and modalities

12.3.1 THE ELECTROENCEPHALOGRAM

The origins of the EEG date back to the end of the 19th century. At this time investigators began to record electrical signals from the brains of living animals. In 1924 Hans Berger (a psychiatrist) successfully recorded electrical potentials from the human brain. Berger continued his work through the thirties and over the succeeding decade electroencephalography saw increasingly widespread application (Gibbs and Gibbs, 1950). Standardization of the common scalp electrode positions was accomplished in 1958 with the publication of 'The ten twenty electrode system of the International Federation' (Jasper, 1958). Measurement and amplification of cortical electrical potentials from the scalp remain the common underlying methods of all brain electrophysiological monitoring. Potentials are conducted from the cerebral cortex to the scalp through the intervening tissue by a process known as volume conduction. The signal becomes progressively attenuated as the distance from the signal generator increases. The impedance and conductance of the intervening tissue (CSF, dura, skull, scalp) vary, and may be further modified by skull fractures, craniotomy flaps, scalp edema and hematomas, so that the voltage detected at an electrode location is not simply a function of the electrode placement, amplifier

settings, and underlying cortical electrical activity (Stockard, Bickford and Aung, 1975).

In the case of the EEG the measured potentials arise spontaneously. Gross reactivity to external stimulation by the examiner (e.g. noise, light, pain) may be tested. Other than routine bandpass filtering and amplification, there is no processing or averaging of signal. The signal is typically on the order of 10–100 μV . Other physiological signals such as the electrocardiogram and electromyogram are typically two to three orders of magnitude greater than the EEG so that great care with respect to technical details must be taken in recording the EEG. This is particularly true in the case of ensuring a low impedance (less than 2–5 $\text{k}\Omega$ at the scalp–electrode interface), selection of appropriate bandpass filters and selection of appropriate reference and ground electrodes. The placement of reference electrodes and the recording montage used will depend to some extent on the purpose of the examination. Cephalic reference electrodes tend to minimize non-cephalic signal, i.e. cardiac or EMG signal. Simultaneous monitoring of other physiological signals (electrocardiogram, electro-oculogram) on separate channels may help identify contamination of the EEG with these signals. Ambient electrical noise (usually 60 Hz) in the environment may also be problematic, and the recording problems are often magnified in the hostile electric environment of the ICU, where there are multiple sources of noise contamination (e.g. other monitors, intravenous pumps, cooling blankets, respirators, etc.). With a combination of improved recording equipment, and some pragmatic bedside modification of potential sources of electrical interference, it is usually possible to obtain technically acceptable recordings. For practical purposes, the frequencies of interest in the spontaneous EEG are below 30 Hz, so that adjustment of the high-pass filter with this in mind can help screen out a lot of electrical noise.

(a) The EEG in traumatic coma

The EEG has been used in traumatic coma since the 1940s. The most common observation has been slowing of background frequencies, with the amount of slowing being approximately proportional to the depth of coma and prognosis (Rumpl *et al.*, 1979; Silverman, 1963; Stockard, Bickford and Aung, 1975; Synek, 1988). Early serial EEG measurements following head injury showed a lag between the onset of profound coma and slowing of the EEG early after injury, and the authors felt that this detracted from the diagnostic value of EEG early after head injury (Dawson, Webster and Gurdjian, 1951). The authors speculated that this might be due to increasing cerebral edema or some metabolic derangement. Given the paucity of clinical responses in profound

coma, the clinical examination may well be insufficiently sensitive to detect evolving metabolic abnormalities. We routinely observe continued worsening (slowing) of the background frequencies of the EEG when monitoring the power spectrum, and this occurs in tandem with loss of evoked potential activity, and reduced arteriojugular oxygen extraction (Figure 12.1). *Other phenomena described in traumatic coma have been the loss of EEG reactivity to external stimuli, such as noise or eye opening, and the loss of normal*

spontaneous variability in the EEG (Bricolo, 1976; Hutchinson et al., 1991; Rumpl et al., 1979; Silverman, 1963; Synek, 1990a, b). Patients where such reactivity has not been totally lost have tended to have better outcomes than those without any evidence of reactivity in the EEG. A more recent study in children with severe head injuries failed to show any difference in prognosis between patients with and without EEG reactivity to external stimulation (Dusser et al., 1989). Patients who have evidence of periodic sleep patterns

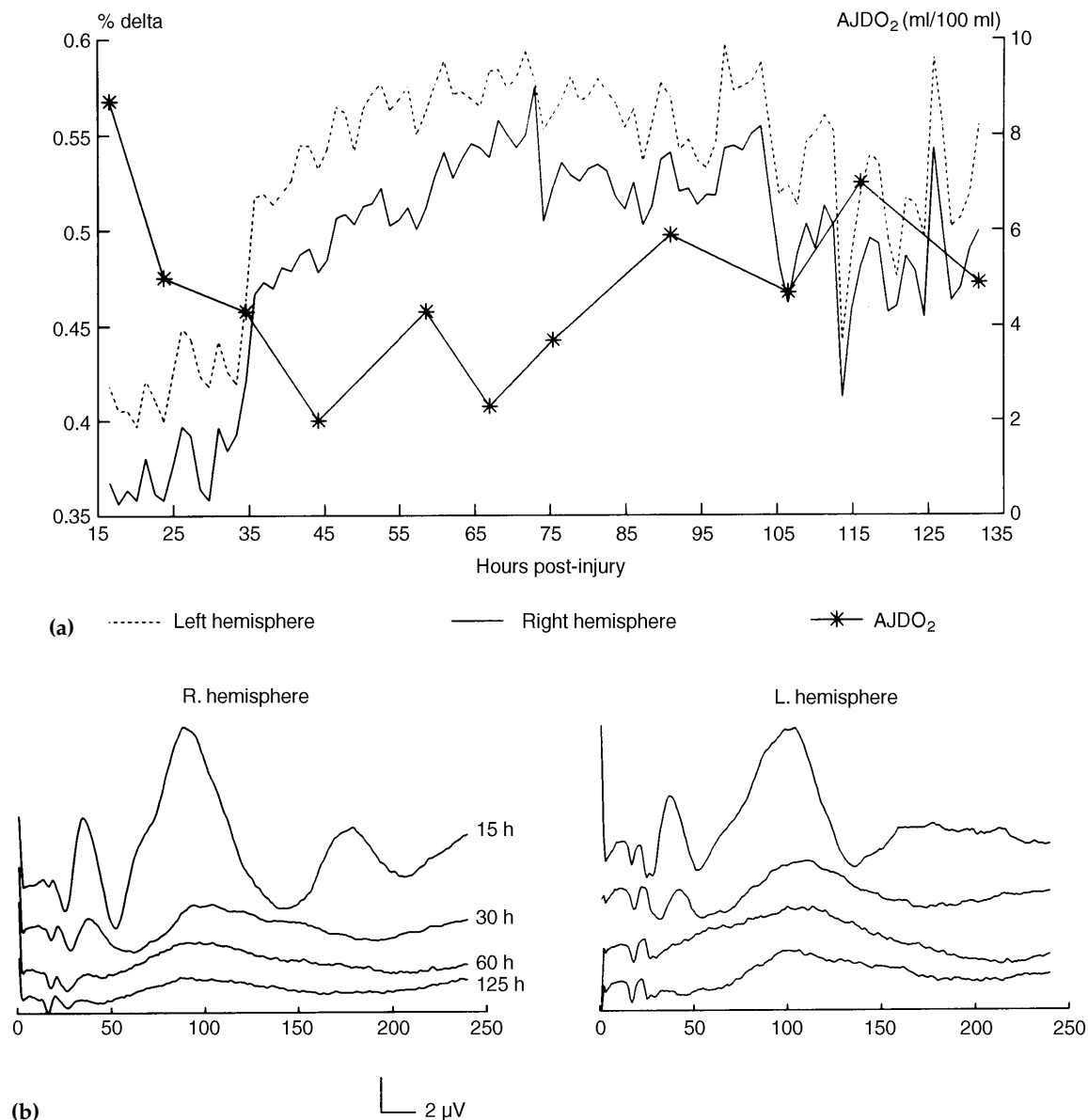


Figure 12.1 (a) Deterioration of EEG activity within 48 hours of severe head injury. Monitoring of the EEG power spectrum was begun immediately after evacuation of an acute subdural hematoma. The graph shows a progressive increase in the relative amount of slow activity (delta) averaged from four leads over each hemisphere. This accompanied by a progressive fall in cerebral oxygen extraction, measured as the difference in oxygen content between a radial artery catheter and a catheter placed in the right jugular bulb. The ICP was not elevated during this period. (b) Median nerve somatosensory evoked potentials recorded from the contralateral hemispheres in the same patient shown in (a). The number of hours post-injury at which the traces were recorded is shown alongside each SSEP.

within the EEG ('spindle pattern coma') tend to have a better prognosis (Bergamasco *et al.*, 1968; Bricolo *et al.*, 1982; Chatrian, White and Daly, 1963). *The most profound pattern of EEG dysfunction in post-traumatic coma, short of complete electrical silence, is burst suppression. Unless it is drug-induced (i.e. barbiturates), and therefore potentially reversible, it is usually a preterminal finding.*

Alpha coma refers to coma in the presence widespread alpha (8–12 Hz) activity. In contrast to normal alpha activity, which occurs over the occiput and can be induced in the normal subject by asking them to lie quietly with the eyes closed, the alpha activity seen in alpha coma is distributed over the entire scalp, and does not vary spontaneously or with external stimuli. Most writers agree that it indicates a poor prognosis (Hari, Sulkava and Haltia, 1982; Obeso *et al.*, 1980; Stockard, Bickford and Aung, 1975; Westmoreland *et al.*, 1975), although this opinion is not unanimous (Sorenson, 1978). Various EEG patterns have been graded according to increasing degrees of abnormality, and the resultant grades are correlated with prognosis (Synek, 1988, 1990a, b). In one series mortality varied from 13% of patients with diphasic spindle activity to 86% in patients with monophasic activity and 100% of patients with electrocerebral silence (Bricolo, 1976). *Care must be taken to avoid misinterpretation of profoundly abnormal EEG patterns (burst suppression, electrical silence) where the possibility of drug overdose exists, as the EEG (and processed versions thereof) is exquisitely sensitive to drug effects. Most patients in modern head-injury practice will have been given drugs that affect the EEG.*

The paper chart EEG is probably most useful following head injury in the diagnosis and management of seizure activity, particularly status epilepticus. Subclinical seizures may continue following the cessation of clinically evident seizure activity or may occur without antecedent tonic-clonic seizure activity. Fortunately, the latter is an infrequent complication of head injury (Bricolo, 1976). Suspicion of subclinical seizures may be raised by the failure of a patient's level of consciousness to improve following the cessation of observable seizure activity. In this circumstance, or if pharmacological paralysis and treatment with large doses of barbiturates are necessary to control post-traumatic status epilepticus, bedside monitoring of the EEG is required to ensure that cortical seizure discharge has actually ceased, in the absence of observable tonic-clonic motor movements. *The cortical seizure discharge itself is harmful to the brain, independent of the additional systemic physiological derangements (hypotension, lactic acidosis) produced by the sustained motor activity (Delgado-Escueta *et al.*, 1982).*

In the years prior to the introduction of modern imaging studies, an effort was made to characterize the accuracy of the EEG in localizing mass lesions. The accuracy of localization was never more than mediocre, i.e. 50–80% (Courjon, 1972; Ravagnati *et al.*, 1982; Rimpl *et al.*, 1979; Silverman, 1963; Stockard, Bickford and Aung, 1975). In cases of minor injury, slowing is often in the posterior leads, no matter where the CT lesion is located (Liguori *et al.*, 1989). Brain mapping techniques appear to improve the localization of structural lesions (see below).

The major drawbacks to EEG monitoring have been the tremendous amount of data generated by the EEG and the requirement for expert interpretation of the recorded data. These factors have driven the efforts to compress and simplify the interpretation of the EEG. The nature of the EEG recording mandates expert interpretation, and this is not available on a continuous basis at the bedside. Offline expert analysis of even a few hours of EEG is difficult because of the volume of data. Also, the necessity for offline expert interpretation blunts the effectiveness of EEG as a monitoring tool. The major advantages of unprocessed EEG are that it remains the only technique for reliably showing transient activity and wave morphology.

(b) The cerebral function monitor

The difficulties with EEG collection and interpretation alluded to above have spawned a number of technologies aimed at data reduction and simplification of interpretation of the EEG. One of the earlier and more popular of these was the cerebral function monitor. The monitor was devised in the period antedating the reduction in the cost and complexity of computer technology and its consequent widespread dissemination. The cerebral function monitor is a simplified strip chart recording of a single channel of EEG activity. The recording is carried out across the vertex in the parietal region. The signal is subjected to a bandpass filter with the passband from 2–15 Hz. The signal is further modified by logarithmic compression of the peak to peak amplitudes and recorded on a very slow strip chart recorder (Maynard, Prior and Scott, 1969). *The technique provides information on whether background EEG activity is increasing or decreasing overall, but little information on the frequency content, or transient phenomena. It is most useful for detecting catastrophic global changes in cerebral function, as might occur with severe hypoxia, hypotension or cardiac arrest (Levy *et al.*, 1980; Schwartz *et al.*, 1973). More recently, the cerebral function monitor has been used as an indicator of the level of cortical metabolism and a guide for the use of anesthetic agents to control intracranial pressure (Procaccio *et al.*, 1988).*

(c) Power spectral analysis of the EEG

The development of the fast Fourier transform algorithm (FFT) provided a computationally efficient (and therefore rapid) means of resolving complex wave patterns such as EEG into their individual frequency components. Combined with the steady reduction in the cost, size, and complexity of computer equipment in the 1970s, this permitted the widespread introduction of equipment that was capable of real-time power spectral analysis (PSA) of the EEG at the bedside. This is currently the most widespread technique of data reduction and simplification of interpretation of the EEG. Bickford pioneered the technique for use with EEG and coined the term 'compressed spectral analysis', based on the technique of displaying the power spectra of the EEG over time (Bickford *et al.*, 1973; Bickford, 1977).

In order to produce an EEG power spectrum one selects an epoch of EEG, typically of 2–4 seconds duration. The FFT resolves the complex EEG waveform into its frequency components and displays the power (amplitude squared) in each frequency bin. (Typically the bins are chosen to be 1 Hz.) In compressed spectral analysis the frequency histogram generated by the FFT is smoothed and displayed as a smooth line drawn through the top of the histogram. Successive lines from each epoch are stacked on top of the previous epoch. The display can be printed out continuously or displayed on a monitor so that trends in the background frequency can be displayed over time. Other display systems employ color or gray-scale coding of the frequency histogram. The speed of the FFT is such that the power spectra can be calculated on a typical microprocessor and displayed in real time, while the data collection system captures and digitizes the next epoch of EEG. Power spectra are displayed for each channel and systems vary in complexity from very small, portable two-channel systems to more complex (and larger) systems with 16-channel capability and more flexible storage and display capabilities.

A further refinement of power spectral analysis of the EEG is brain electrical mapping, which involves the interpolation of the power spectra values between electrode positions on the scalp and the display of these values as contour maps (Duffy, Burchfiel and Lombroso, 1979). This technique may improve the localization accuracy of EEG for structural lesions. In one recent study the accuracy of localization of structural lesions (abscess, glioma, hematoma) was 100%. There was a tendency for the lesions to appear larger with brain mapping, perhaps reflecting an area of physiological abnormality that was larger than the anatomic lesion. Ischemic lesions may be shown that are not evident with CT/MRI imaging (Jerret and Corsak, 1988).

From a practical perspective, brain mapping is not likely to displace CT imaging in the diagnosis of acute operable structural lesions, because of the difficulty in distinguishing physiological abnormalities associated with non-operative structural lesions, from electrical abnormalities emanating from the brain surrounding operable structural lesions. However, EEG topographic mapping or other techniques of electrical function monitoring may be useful in showing the progression of existing lesions, or providing early evidence of development of delayed structural lesions.

The above techniques considerably compress and simplify the interpretation of the EEG and these reasons alone are often sufficient to justify their use. In addition, quantification of the EEG allows for statistical analysis of EEG data and permits graphic displays of frequency trends over prolonged periods of time. The degree of quantitative frequency resolution achievable by PSA is not something that can be duplicated by visual interpretation of time domain analog EEG signal. There are a number of trade-offs for these advantages. Probably the most important is that the FFT technique averages the signal over the duration of the epoch. While this makes no difference for the analysis of background frequencies, it does remove the ability to detect transients such as seizure spikes. In addition, it removes any ability to look at the morphology of EEG waves. For example, a seizure discharge may not appear any different from ordinary background activity of the same frequency, unless the seizure discharge involves some major frequency shift or change in amplitude. Even if these occur, it will still be necessary to examine the raw EEG tracings to confirm the presence of seizure activity, based on the morphology of the raw EEG. The inclusion of all recorded signal in the Fourier transform makes the incorporation of physiological or external electrical noise in the transformed EEG potentially problematic. A certain amount of experience looking at raw EEG is necessary to make this distinction. The ability of the monitoring equipment to display the raw EEG tracing to detect ECG or other non-EEG signal is essential. Selection of grounding and reference leads can often be optimized to minimize inclusion of non-EEG signal.

(d) Power spectral analysis in traumatic coma

A number of authors have looked at the prognostic capabilities of PSA in traumatic coma. The most frequently used criterion for predicting a poor prognosis was a pattern of unvarying activity with the major frequency component in the delta (1–3 Hz.) band. Variable spectral patterns were generally associated with a better prognosis (Bricolo *et al.*, 1978; Sironi *et al.*, 1982). This variation probably represents the PSA equivalent of spontaneous or induced varia-

bility seen in the raw EEG and previously associated with a good prognosis. Other authors have found that the persistence or return of a peak in the alpha or theta frequency band indicated a good outcome from traumatic coma (Cant and Shaw, 1984; Steudel and Kruger, 1979). *Karnaze, Marshall and Bickford (1982) found that the compressed spectral array was equivalent in prognostic accuracy to the Glasgow Coma Score. The background frequencies of the EEG measured with power spectral analysis are highly correlated with the Glasgow Coma Score and the correlation improves with increasing time postinjury (Moulton et al., 1988).* This improvement in correlation with the depth of coma is probably due to the lag between injury and slowing of the background frequencies described previously with conventional EEG. As noted above, the delayed slowing takes place in association with progressive disturbance of other electrical function parameters, and measurements of oxygen extraction (Figure 12.1).

In our experience with monitoring the EEG power spectrum we have found that the overall trend in background frequency, viewed over several days, usually mirrors patient improvement or deterioration. We monitor the relative amplitude within the four customary frequency bands (i.e. the fraction of total power contributed by the delta, theta, alpha and beta frequency bands) rather than the absolute power in each band. This tends to reduce the amount of variability over time and makes trends more easily discernible (Figure 12.2). In general there is a steady increase in the amount of slow (delta) activity from the time of initiation of monitoring in patients who die, or survive with severe disabilities. Patients who survive with a functional outcome usually either show reduction in the amount of slow activity, or little or no net change over time. Using discriminant analysis of frequency content with the 'jack-knife' technique of error estimation we found that the prognostic accuracy for good or moderate outcome *versus* death, vegetative survival, or severe disability was 75%. There were a number of falsely pessimistic predictions because of transient reversible complications that were reflected in the EEG (Moulton et al., 1988). With the luxury of viewing the PSA trends *post hoc* after several hours (or days) post-injury, these trends are usually easily seen. However, because of the variability inherent in the measure, particularly in patients who do well, the meaning of background frequency changes at any given moment in time is much less clear (Figure 12.3). *For this reason, although we do monitor the EEG power spectrum continuously, we find the information much less useful than that obtained from evoked potentials, which have much less variability over time.* Occasionally, in cases of a significant global insult, processed EEG may more

clearly reflect the impact on cerebral function than other electrophysiological data (Figure 12.2(a)).

Other information available from analysis of the EEG in the frequency domain includes phase and coherence data. These reflect the lead or lag time between shared activity in different regions of the brain, and the amount of shared activity between two regions in the brain, respectively (Thatcher et al., 1989). Generally with increasing severity of head injury one sees increased coherence and reduced phase. The latter may be reflective of subcortical white matter damage and tends to be more stable over time than measures of relative or total power, possibly indicating a degree of resistance to acute injury dynamics (brain edema, intracranial pressure etc.). Use of phase and coherence data from the EEG significantly improves the prognostic accuracy of EEG following head injury, possibly reflecting better measurement of the predominant pathology in blunt head injury, i.e. axonal damage in the white matter of the hemispheres (Thatcher et al., 1991).

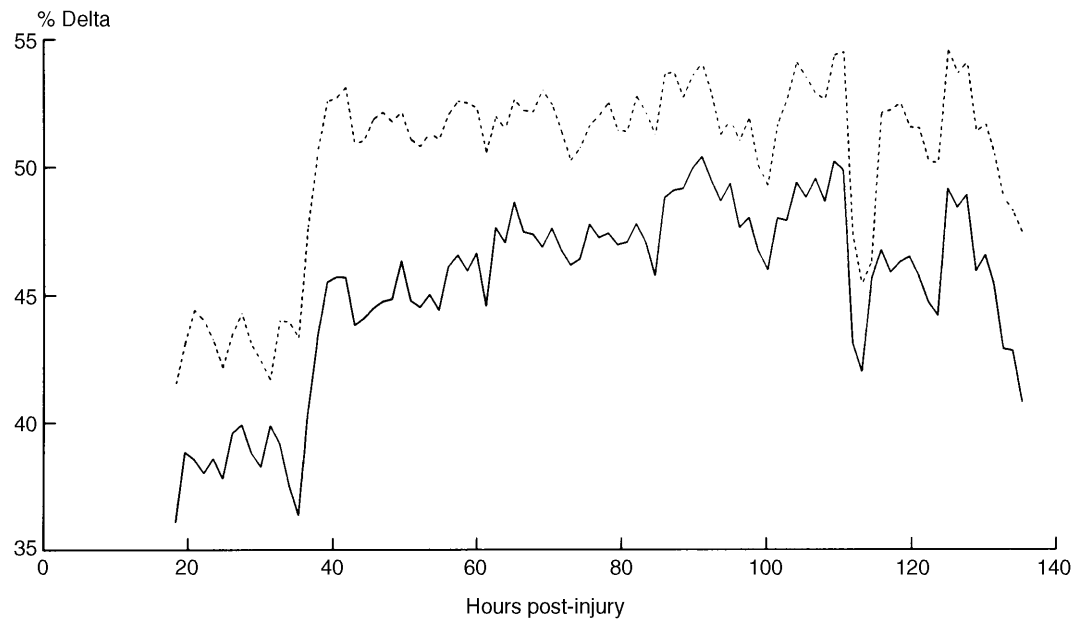
12.3.2 EVOKED POTENTIALS

(a) Technical principles

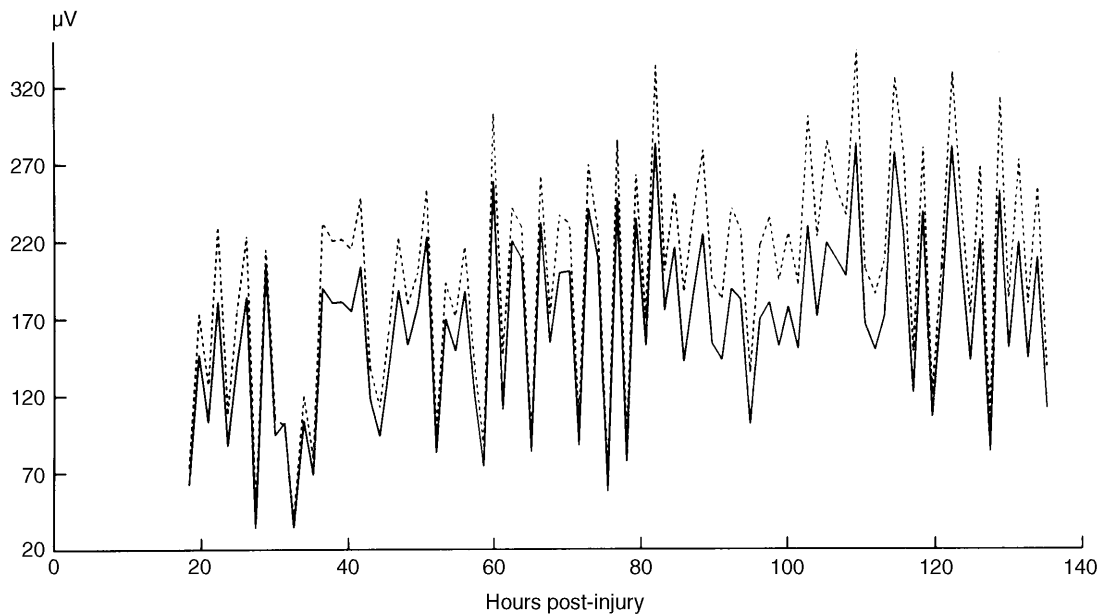
In contrast to EEG, which is a measurement of the spontaneous electrical activity of the cerebral cortex, evoked potentials measure cerebral hemispheric and/or brain-stem responses to stimulation of a sensory receptor (i.e. visual, auditory or somatosensory). The typical response is of the order of 0.5–5 μV as opposed to 10–100 μV for spontaneous cortical activity (i.e. EEG). A single evoked response is therefore lost in the background random EEG activity. Signal averaging techniques are required to demonstrate the response. Repeated stimuli are used at fixed intervals that are dependent on the particular evoked response to be studied. The evoked responses, which occur at a fixed time from the stimulus, are preserved by the averaging process, whereas the background EEG, which occurs randomly with respect to the stimulus, is canceled out by averaging. Evoked electrical potentials arrive at the scalp by two processes: conduction along the fiber tracts of the sensory pathway in question and volume conduction. For practical purposes, volume conduction is virtually instantaneous with respect to conduction along axons, so that potentials arising from synaptic relays along the course of the sensory pathways arrive in an orderly fashion from distal (brain stem) to proximal (cortex).

(b) Visual evoked potentials

These are generally evoked by using a strobe light or checkerboard stimulus. *They yield information about*



(a) ····· Left hemisphere — Right hemisphere



(b) ····· Left hemisphere — Right hemisphere

Figure 12.2 (a) EEG power spectrum monitoring in a 50-year-old man following severe closed head injury. This man aspirated shortly after injury and developed severe bilateral aspiration pneumonia and ARDS. The monitored parameter is the relative amount of slow activity averaged from four leads over each hemisphere. At 36 hours post-injury the patient's blood pressure fell to 60 mmHg and the P_{O_2} fell to 60 mmHg on 100% oxygen. The large increase in slow activity occurred at that time. Two days later a CT scan showed large bilateral frontal infarctions around two small contusions. The patient died at 1 week post-injury. (b) EEG power spectrum monitoring in the same patient. The monitored parameter in this instance is the absolute amplitude in the delta band rather than the relative amplitude. The large amount of variability from hour to hour effectively conceals the increase in slow activity seen in (a).

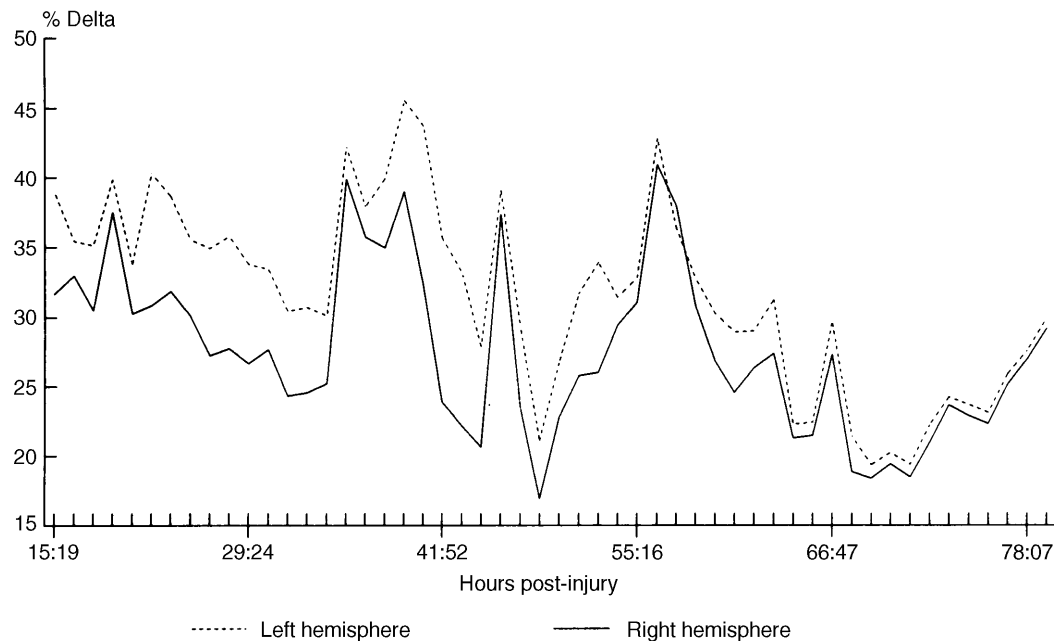


Figure 12.3 The EEG power spectrum monitored over 3 days post-injury in a 40-year-old man following evacuation of an acute subdural hematoma. The relative amount of slow activity (delta) is averaged from four leads per hemisphere. The overall trend is one of decreasing slow activity and the patient went on to a functional recovery. The large amount of variability over time, particularly in the mid-portion of the recording, makes the real-time interpretation of the data difficult. These fluctuations did not occur in the presence of any detectable systemic physiological perturbation, nor any ICP elevation. They may represent diurnal variation in the EEG in a patient with a good prognosis.

the functional integrity of the visual apparatus and may be useful in indicating the presence of visual loss in a comatose patient (Feinsod and Auerbach, 1973; Mahapatra and Bhatia, 1989). In terms of predicting the outcome from head injury, they are less useful than somatosensory evoked potentials (see below) (Lindsay *et al.*, 1981), although they do marginally improve the prognostic accuracy of evoked potentials when used in combination with other evoked potential modalities (Narayan *et al.*, 1981).

(c) Brain-stem auditory evoked potentials

Brain-stem auditory evoked potentials (BAEPs) have been used in a continuous monitoring application and have been shown to progressively deteriorate in the preterminal stages of coma following head injury (Bertrand *et al.*, 1987; Garcia-Larrea *et al.*, 1987). This deterioration is not necessarily related to uncontrollable intracranial pressure (Garcia-Larrea *et al.*, 1992). *In our experience with hourly monitoring of both somatosensory evoked potentials (SSEPs) and BAEPs we have found that SSEP deterioration up to and including complete loss of cortical activity precedes loss of peaks in the BAEP (Figure 12.4). The stage of brain dysfunction that precludes the possibility of a functional outcome may well occur before there is significant change in the BAEP. This probably*

*explains the frequent occurrence of poor outcome from head injury in the presence of normal or nearly normal BAEPs (Cant *et al.*, 1986; Cant, 1987; Lindsay *et al.*, 1981; Papanicolaou *et al.*, 1986).* While the absence of BAEP activity certainly predicts a poor outcome, the presence of brain-stem responses does not necessarily predict survival or a functional outcome. *The quality of survival depends on cerebral hemispheric integrity, and this is not something that is measured by the BAEP.* Near field auditory potentials have been found to be of greater value in predicting functional outcome (Lindsay *et al.*, 1981; Ottaviani *et al.*, 1986), but these are not commonly done and cortical functional integrity is more commonly measured with somatosensory evoked responses.

BAEPs are usually evoked by using a click stimulus delivered to a single ear using an earphone or earplug apparatus. Optimal recordings are obtained from C₀ referenced to the ipsilateral ear. The duration of recording of the response is typically 10 ms. Five peaks are produced as the stimulus traverses the brain stem. Wave I is thought to arise from the auditory nerve itself. Waves II and III arise from the caudal pons and waves IV and V from rostral pons and mesencephalon (Legatt, Arezzo and Vaughan, 1988). The wave I-V interpeak latency therefore gives an indication of the transit time of an electrical signal across the brain stem. Abnormalities of BAEP conduction time do

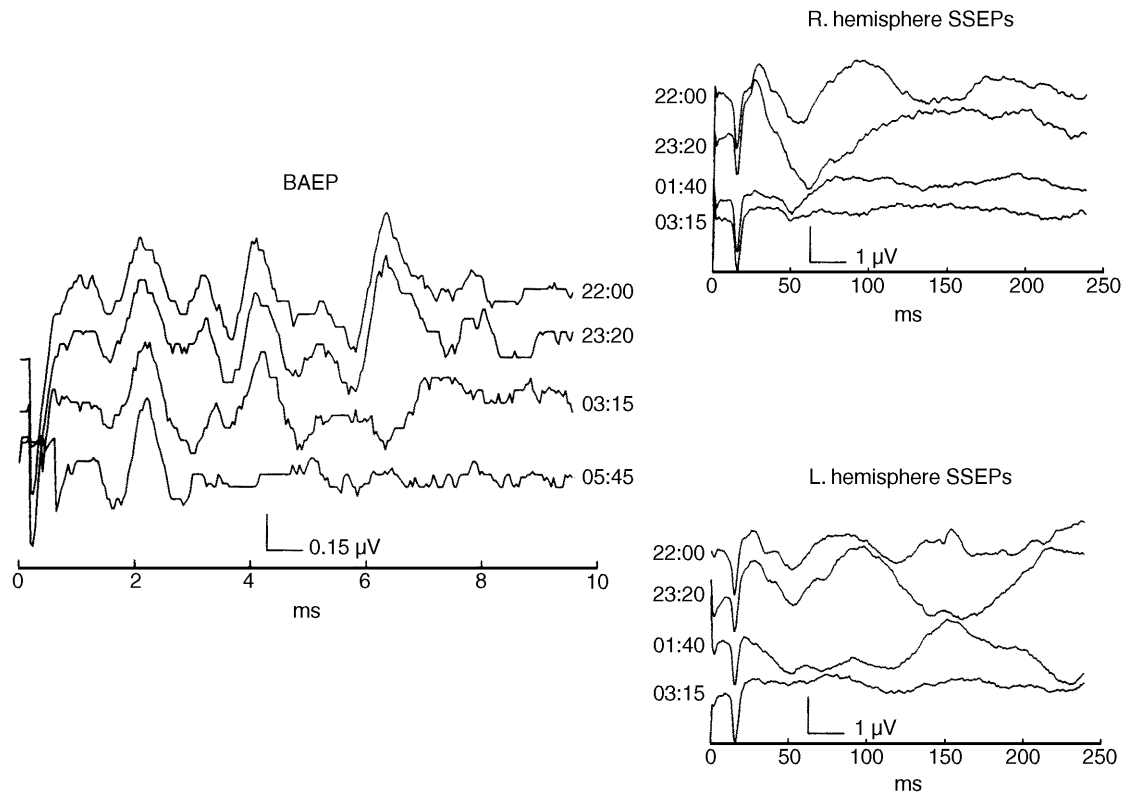


Figure 12.4 Serial BAEPs and SSEPs (positive waves down for both) in a patient with a severe diffuse head injury. Monitoring was begun at approximately 5 hours post-injury at 22.00h. There is progressive loss of cortical SSEP activity over time from levels initially compatible with good quality survival. At 03.15h cortical activity has been absent bilaterally for at least 90 minutes. At this time the BAEP shows only some prolongation of the I–V interpeak latency. Waves III–V disappear some 2.5 hours later. ICP was maintained at less than 25 mmHg during the period in which cortical SSEPs disappeared. The BAEPs were lost when the ICP subsequently became uncontrollable.

correlate with poor outcome, but the correlation is not as good as that of the central conduction time of the somatosensory evoked potential (Cant *et al.*, 1986; Lindsay *et al.*, 1990). *In head-injury patients the entire BAEP, including wave I, may be absent because of end-organ damage (e.g. petrous bone fracture). Absence of wave I following closed head injury is a fairly common circumstance and prevents satisfactory interpretation of BAEPs in a significant number of patients.* In the situation of an absent wave I one cannot reliably draw any conclusions about brain-stem function because of the possibility that its absence is due to end-organ damage rather than impaired brain-stem function (Cant, 1987). In contrast, if waves II–V are absent and wave I is present, this indicates severe brain-stem disturbance and indicates a very poor prognosis (Cant *et al.*, 1986; Garcia-Larrea *et al.*, 1992; Hall, Huang-fu and Gennarelli, 1982). BAEP abnormalities correlate with pupillary abnormalities and other clinical evidence of brain-stem dysfunction but do not correlate with motor posturing (Barelli *et al.*, 1991; Greenberg *et al.*, 1977; Lindsay *et al.*, 1990).

(d) Somatosensory evoked potentials

Somatosensory evoked potentials (SSEPs) are generated by stimulating a peripheral nerve containing large myelinated sensory fibers, usually the median at the wrist or the posterior tibial at the ankle. The impulses are conducted centrally through the dorsal column system, traverse the brain stem and produce a series of peaks from the cerebral hemisphere. The number and morphology of the latter depend in part on the duration of the recording. The standard recording montage for intermediate and long-latency activity consists of recording just posterior to the C₃ and C₄ electrode positions (C₃' and C₄') referenced to linked ears. Additional electrode positions at Erb's point (located over the brachial plexus) and over the spinous process of the second cervical vertebra are used if one wishes to examine the somatosensory far-field potentials in greater detail. This is often done for precise recording of the central conduction time, i.e. the transit time of the somatosensory response from the caudal medulla to the primary somatosensory cortex in the postcentral gyrus.

The naming convention for SSEP peaks is based on the polarity (positive – P or negative – N) and the post-stimulus latency in milliseconds. The P₁₅ is the first deflection seen in the SSEP and arises from the caudal medulla. The N₂₀ is the first cortical peak and is felt to arise from the postcentral gyrus. The initial cortical peak may have a frontal component and parietal and frontal components may be lost independently of each other following injury (Gütling *et al.*, 1993). Later peaks likely arise from association cortex or reverberating circuits between the cortex and subcortical structures (Greenberg and Ducker, 1982; Yamada, 1988). While there is a reasonably established consensus about the origins of the P₁₅ and N₂₀, there is no well-established consensus regarding the site of origin of the later peaks. These later peaks also have considerably more variability in their latencies, both between and within patients (Greenberg and Ducker, 1982; Yamada, 1988).

Unlike the fairly constant morphology of the BAEP and the relatively constant measure of the wave I–V latency, the variability of the SSEP leads to some problems in classifying/grading the degree of abnormality of SSEP responses. The one exception to this is the use of the central conduction time, as the peaks on which calculation of this value depend are quite constant (Hume and Cant, 1981; Lindsay *et al.*, 1990; Ruml *et al.*, 1983; Whittle, Johnston and Besser, 1987). However, there may be some loss of sensitivity in detecting SSEP change because the method ignores cortical activity occurring after the N₂₀ (Moulton, Konaciewicz and O'Connor, in press). *Our work and that of others, in cases of post-traumatic and post-anoxic coma, suggests that, while the absence of early cortical activity is an excellent predictor of survival or death, it is activity occurring at or beyond 70 ms that more accurately reflects the probability of a good quality outcome (see below).* A number of other approaches to grading SSEPs have been described, including fairly complex (and subjective) grading schemes based on the presence or absence of peaks at particular latencies and the number, amplitude and morphology of these peaks (Greenberg *et al.*, 1977; Rappaport *et al.*, 1981). Other approaches have included simple peak counts (Lindsay *et al.*, 1981), or grading based on the longest latency peak present in the SSEP response (Moulton *et al.*, 1991; De La Torre *et al.*, 1978). There is a substantial degree of inter-correlation between these parameters, the more subjective grading schemes and the central conduction time. Consequently the results are similar when these grading paradigms are employed in the clinical setting, i.e. correlation with patient outcome (Moulton, Konaciewicz and O'Connor).

Over time the SSEP has come to be recognized as the single best predictor of outcome among the

*available evoked potential measurements (Cant, 1987; Lindsay *et al.*, 1981, 1990). This is very probably due to the ability of the SSEP to sample the function of the entire intracranial neuraxis from brain stem to cortex, and the heavy dependence of survival and the quality of survival on the integrity of both brain stem and cerebral hemispheric function.* The response is usually relatively easy to record and, unlike the BAEP, is seldom lost on account of associated injuries. The two exceptions are injury to the spinal cord or brachial plexus (the latter in the case of upper extremity evoked responses).

The absence of any activity beyond the P₁₅ is highly predictive of death. The presence of increasingly long latency peaks correlates with increasing quality of survival. Presence of SSEP activity beyond 50–70 ms post-stimulus appears essential for functional survival (De La Torre *et al.*, 1978; Moulton *et al.*, 1991). This appears to be true in cases of post-cardiac-arrest anoxic coma (Madl *et al.*, 1993), in addition to post-traumatic coma. In our hands the sensitivity, specificity, and positive predictive value for the bilateral absence of activity at or beyond N₇₀ in predicting death or vegetative survival were 0.61, 0.95 and 0.89 respectively. The sensitivity, specificity, and positive predictive value of bilateral preservation of activity at N₇₀ or later in predicting good outcome or moderate disability were 1.0, 0.75 and 0.55 respectively (Moulton *et al.*, in press). The poor positive predictive value for good outcome or moderate disability seemed to be due to the effect of age on outcome. Elderly patients tended to do poorly even in the presence good evoked potentials, because of the independent effect of age on outcome from head injury (Shedden *et al.*, 1990). On the other hand, although bilateral intermediate and late cortical SSEP activity is not sufficient grounds for good outcome or moderate disability, it is a necessary one. *In our hands no patients had a good outcome or moderate disability who did not have bilateral intermediate and late cortical activity. Unilateral or bilateral absence of activity has a high positive predictive value for severe disability, vegetative survival or death. The effect of bilateral absence of activity is independent of age (Moulton *et al.*).*

Early recordings of SSEPs tended to be done on a sporadic basis, often 48–72 hours postinjury or more. These single or infrequent studies were adequate to establish the prognosis from injury, but were not adequate for patient monitoring. When serial testing was initiated, it became apparent that changes in SSEPs do occur. Newlon *et al.* felt that deterioration in SSEPs was due to secondary insults such as raised intracranial pressure (ICP), hypoxia or delayed hematomas (Newlon *et al.*, 1982). Lindsay *et al.* also detected changes in SSEPs recorded early after injury and 48–72

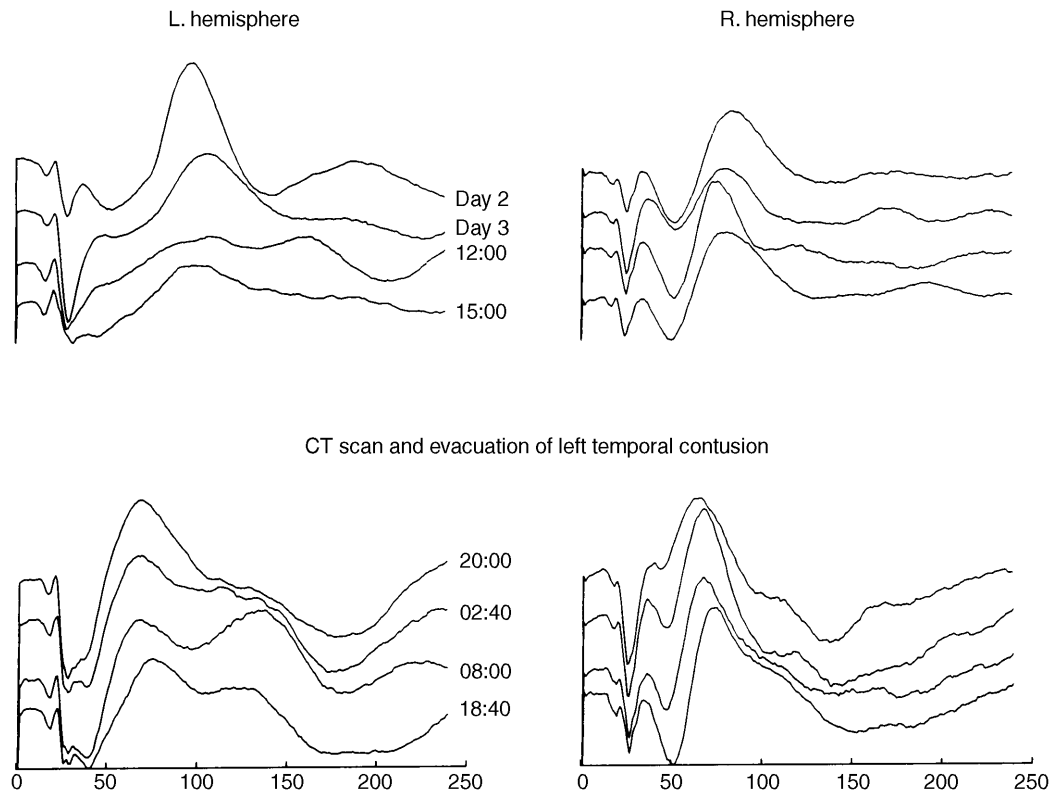


Figure 12.5 Serial somatosensory evoked potentials in a man following evacuation of an acute subdural hematoma. On the fourth post-injury day loss of SSEP activity above 25 ms latency on the left side triggered a repeat CT scan. A small left temporal contusion present at the time of admission had increased in size and a left temporal lobectomy was subsequently undertaken. There was immediate recovery of SSEP activity following operation. The ICP never exceeded 20 mmHg prior to evacuation of the contusion. The labels on the tracings are the time post-injury (days, 24-hour clock beginning on fourth day).

hours later. They did not speculate on reasons for these changes, but simply stated that early SSEP recordings were not as reliable for determination of prognosis (Lindsay *et al.*, 1990). *In our own recordings of SSEPs, done on an hourly basis, we found that changing SSEP activity was extremely common, with deterioration occurring in approximately two-thirds of patients whose monitoring was begun within 24 hours of injury. These changes occurred bilaterally (Figures 12.1, 12.4). In the majority of patients no clearcut secondary insult could be identified to account for the deterioration.* In a much smaller group of patients we identified unilateral changes in SSEPs occurring as the result of evolving focal pathology (Figure 12.5). A small number of patients showed improvement following injury (Moulton *et al.*, 1991). *We have been unable to relate deterioration in SSEP values to levels of ICP (Konasiewicz, Moulton and Shedden, 1993; Moulton *et al.*, in press). The deterioration does seem to correspond to reduced levels of transcranial oxygen extraction (i.e. the arterio-jugular oxygen difference) possibly implicating a role for perturbation of oxidative metabolism in the genesis of SSEP deterioration (Figure 12.1; Moulton *et al.*, in*

press). The correspondence between SSEP deterioration and AVDO₂ decrease is not absolute, and the observed deterioration in SSEP activity is probably multifactorial.

(e) Multimodality evoked potential monitoring

The prognostic accuracy of the SSEP may be improved to some extent by monitoring visual and brain-stem auditory evoked responses as well (Narayan *et al.*, 1981). The additional improvement in accuracy is marginal and may not justify the increased effort and expense of monitoring other electrophysiological parameters, including the EEG or its power spectrum. Perhaps the one exception to this is the BAEP, as it does have the desirable feature of being impervious to the effects of the large doses of barbiturates that are occasionally necessary to control refractory increases in ICP (Newlon *et al.*, 1983). *While relatively resistant to the usual analgesic or sedative doses of narcotics, cortical SSEP responses can be abolished by large doses of barbiturates.* From time to time other electrical function measurements may be useful in diagnosing specific complications such as seizures

(EEG) or visual loss in an uncooperative patient (VEPs), but the workhorse evoked potential for prognosis and monitoring will probably remain the SSEP. *In patients who die, loss of cortical somatosensory evoked potentials (a highly reliable indicator of poor outcome) precedes electrocortical silence by hours or even 1–2 days (Ganes and Lundar, 1988).* A direct comparison of the prognostic capability of EEG and somatosensory evoked potentials has shown the latter to be clearly superior (Hutchinson, 1991). **Motor evoked responses have not been shown to be useful in predicting outcome from coma (Zentner and Rohde, 1992).**

12.4 Conclusions

At the present time the value of evoked potential examination is proven for prognostication in cases of traumatic coma. In ordinary circumstances the accuracy of prediction is approximately that which is achievable by clinical measures alone, so that measurement is probably not cost-effective in this circumstance. However, in cases where clinical monitoring is difficult or impossible, e.g. pharmacological paralysis for respiratory or ICP management, information from evoked potentials may be extremely useful in deciding on continuation or cessation of very aggressive therapy.

The need for on-line, objective electrophysiological monitoring of brain function seems self-evident. However, the combination of the expense, and difficulty of use of such equipment on the one hand, and our limited ability to usefully intervene in patients with declining neurological status on the other, have tended to restrict the application of such monitoring to university-affiliated tertiary referral centers. Even in this limited application, these techniques will remain useful in the immediate future for defining important pathophysiological sequelae of injury, and distinguishing these from epiphenomena. With the advent of new therapies for closed head injury, further improvement in monitoring equipment and techniques and a reduction of equipment cost, it is likely that brain electrical function monitoring will play an increasingly important role in evaluating and later directing the application of these new therapies.

12.5 References

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