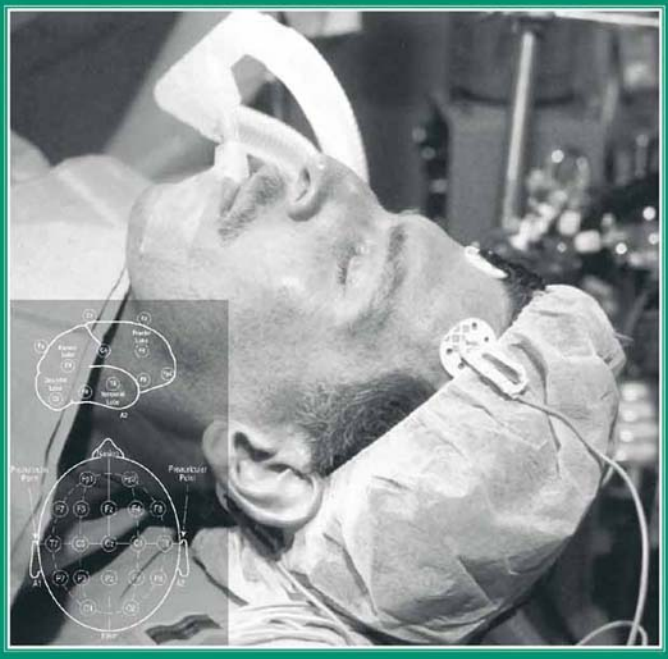
Cerebral Monitoring in the OR and ICU

Enno Freye



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PREFACE

The evaluation of an ICU patient's degree of consciousness has taken on great importance. The problem of unintended intraoperative rivival and compensation has resulted in the need for monitoring the level of unconsciousness with instruments that measure the patient's cerebral activity rather than vital signs (arterial pressure, cardiac rate, tear secretion, etc.). In addition, the need for salvaging organs for transplantation requires the anesthesiologist to understand cerebral mechanisms to diagnose brain death before the disappearance of vital signs which renders the organs useless for transplantation. In the final analysis the physician has had to change his vision of cortical activity considered, if not strictly indispensible, at least of secondary importance relative to the hemodynamic consequences to the patient. The problem is even more complex in those nations where the teaching of anesthesia and reanimation is combined, presenting the physician with the twofold chore of cerebral monitoring to prevent intraoperative awakening and to detect brain death.

Technological innovation has created simple, precise instruments to replace ECG devices which are subject to artifacts caused by patient movement or interference from other electronic instruments in the operating room or ICU. However, the use of modern devices such as the bis-monitor, entropy, etc. is not widely taught in university courses, forcing the anesthesiologist to embark on a disorganized study of the various instruments, often not accompanied by an understanding of cerebral activity. Prof. Freye's book is an organized treatment of cerebral activity which offers a clear explanation of the generation of cerebral impulses and the potential value that cerebral monitoring holds for patients. Although many complex algorithms appear in the book, the text explains modern monitoring techniques with such simplicity that even physicians with little knowledge of mathematics and physics will easily understand the subject. Moreover, the study of evoked potentials, which is invaluable in orthopedic surgery and many other pathologies treated in Intensive Care, is presented clearly and logically. Attractive graphics contribute to the pleasure of reading the book, making the subject less tiring for readers who are confronting the subject for the first time. Physicians who are accustomed to using the ECG will also find that the close examination of this topic alone makes the book worthwhile.

The *Journal of Clinical Monitoring and Computing* is pleased to present Prof. Freye's book because it is in perfect harmony with our publication's goal of assisting clinicians in the daily use of the most advanced monitoring and computer techniques in patient care.

Vincenzo Lanza
Editor-in-Chief, *Journal of Clinical Monitoring and Computing*

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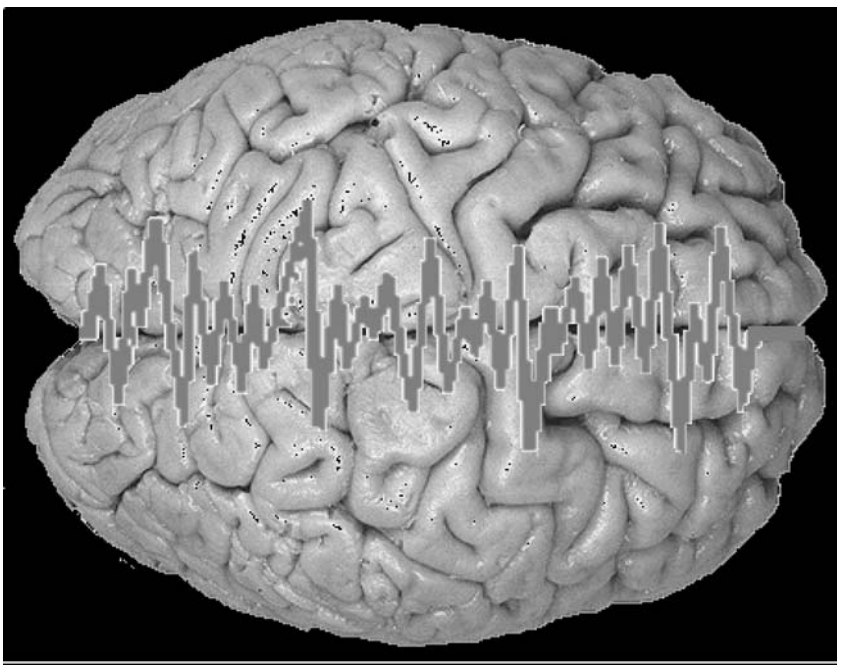
CEREBRAL MONITORING IN THE OPERATING ROOM AND THE INTENSIVE CARE UNIT: AN INTRODUCTORY FOR THE CLINICIAN AND A GUIDE FOR THE NOVICE WANTING TO OPEN A WINDOW TO THE BRAIN

*Enno Freye, MD, PhD and Joseph V. Levy, PhD**

PART I: THE ELECTROENCEPHALOGRAM



Authors address: Clinics of Vascular Surgery and Renal Transplantation, Heinrich-Heine-University, Düsseldorf, Deichstrasse 3a, 41468 Neuss-Uedesheim/Germany.
E-mail: enno.freye@uni-duesseldorf.de

*Department of Physiology, University of the Pacific, San Francisco, California 94115, USA

PREFACE. While there is an increasing body of knowledge in regard to central nervous system function and/or the mode of action of centrally active agents on neuronal function, little is done to develop new techniques on how to measure such changes. Also, monitoring of the cardiovascular system in the past has made extensive progress especially when it comes to evaluate the failing heart. In contrast monitoring of the central nervous system is only done in rare cases where operative procedures likely impede nervous function integrity. Since in the past decade the aging population undergoing operation has rise considerably, the risk of cerebral malperfusion or minute signs of degradation of the aging central nervous system (CNS) to anesthetics and agents being used in the operation room (OR) or the intensive care unit (ICU), needs continuous monitoring of an organ which presents the highest vulnerability and is likely to deteriorate faster than the cardiovascular system. In spite the rapid improvement in technology regarding the electroencephalogram (EEG) and evoked potential monitoring, physicians still are reluctant to use a technology on a routine base, which will give them insight information into brain function and activity. Such "*windows to the brain*" now not just are reserved to specialists working in the area of neurology and/or psychiatry. More so, cerebral monitoring is getting an integrated part in the overall therapy in patients undergoing operation or who need ventilatory support in the ICU as it effects the well-being and the outcome. The present book therefore, is intended for the practitioners who work with the patient, guide the clinician in his decision making and outlining those situations where cerebral monitoring presents an integrated part in the diagnosis and therapy of patient care. Without going too much into the technical details, representative cases underline the potential use of cerebral monitoring in the underlying clinical situation where either the patient presents borderline perfusion of the CNS, undergoes vascular surgery, or where monitoring of cerebral function in the intensive care in a head trauma patients is an integrated part in therapy.

The book therefore is meant for all those clinicians who have to deal with the CNS in a day-to-day situation. This may be the anesthesiologist, the surgeon, the intensive care therapist, the nurse anesthetist as well as all other medical personal involved in intensive care therapy. The aim of the book therefore is to outline the possibilities, the limitations, and the options for therapy when the *windows to the brain* are opened, how to interpret the data in the light of other physiological parameters and aid the user in the technical details of how to avoid artifacts in recording which may have an impact on final decision making. Therefore, emphasis is placed on the electrode placement, artifact and electrical noise reduction, as well as data interpretation so that cerebral function diagnosis can be made on reliable grounds. The following serves as an introduction to and as a reference guide for *Cerebral Monitoring in the OR and the ICU*:

- Gives complete coverage of EEG power spectra analysis.
- Describes in detail the EEG machines available to be used in the OR and ICU setting.
- Describes in detail the major features of EEG power spectra and evoked potential measurements, including amplifiers, filter setting and microprocessor algorithm for data reduction.
- Gives suggestions for assessing and improving signal quality, including noise and artifact rejection, which usually are encountered in the operation room and the intensive care unit, both of which can be considered as electrically contaminated.
- Gives examples of EEG power spectra and evoked potential monitoring related to different types of anesthesia, in coma, after head trauma, and for the detection of ischemic events.
- In addition, gives complete coverage of those machines being available for the OR and the ICU, including a list of parameters regarding latency and amplitude in evoked potential measurement.

As an introductory, recommendations are given for the novice to start cerebral monitoring and guide the beginner in setting up cerebral monitoring in the clinical environment.

KEY WORDS. EEG power spectral analysis, BIS Entropy Patient State Index, Narcotrend, Hypnax anesthetic effects, CEA

INTRODUCTION

Quantified electrophysiology refers to the computer-based acquisition, display, storage, and analysis of EEG or stimulus-evoked potentials (EPs). The data can be evaluated in the time domain or converted to the frequency domain. The latter permits analysis of the EEG and EP based upon the frequency components of the signal. The spatial distribution of the dependent variables is frequently presented as two-dimensional topographic color maps. Quantified electrophysiology has been advocated as an adjunct to traditional EEG and ER recordings. It offers a method by which to quantify aspects of the EEG that have been routinely evaluated qualitatively. The promising advantage of quantified electrophysiology is the ability to quantify aspects of the EEG and evoked responses that are not observable from visual inspection of the time-domain record and that may convey information concerning cerebral function, correlates of cognitive activity, neurophysiologic mechanisms, spatial localization of cortical generators, and diagnostic classification. The data lends itself to statistical analysis for evaluating objectively within-subject changes during anesthesia-induced changes or individual comparisons to age-adjusted normative databases. The advances in microprocessor technology have driven in part the emergence of quantified electrophysiology. The hardware and software requirements for signal acquisition, display, analysis, and storage that were once only available on expensive mainframe systems have been implemented on low-cost personal computers. This has resulted in an increase in the accessibility of this technology and an expansion of the clinical and experimental applications of quantified electrophysiology. Along with the proliferation of this

technology are controversies concerning various aspects of the methodology and its application, to data acquisition techniques, the physiological significance of the variables derived from spectral analysis, the spatial relationship between scalp potentials and cortical generators, the limitations of topographic mapping, and the appropriate statistical analysis of the multiple variables derived from quantitative electrophysiology. The present book will deal the methodology and applications of quantified electrophysiology. The techniques of data acquisition will be presented from the perspective of their effects on frequency analysis measures: power, coherence, and phase and their usefulness in the clinical setting. Finally, individual examples and group comparisons will be presented.

The acquisition of EEG for quantitative analysis should adhere to the standards established for traditional EEG monitoring and should include the ability to view the EEG during collection on a polygraph or a high-resolution display. This permits the identification of artifacts and insures the integrity of the input data. Most applications use the 10–20 international system of electrode placement for EEG acquisition. Some workers to increase spatial resolution and to meet the mathematical assumptions of data manipulation and analysis have advocated larger numbers of electrodes. However, since anesthetics when given to patients will affect all neuronal cells, in most instances it is only necessary to derive to channel recording Additional electrodes to monitor extracerebral contaminants of the EEG such as eye movement, EKG, and muscle activity are only essential in pharmaco-EEG studies. Amplification, filtering, and digitization determine the frequency characteristics of the EEG and EP and the source of potential artifacts. The acquisition parameters must be chosen with an understanding of their effects on signal acquisition and subsequent analysis. Amplification increases the amplitude of the EEG or ER signal from the microvolt level at the scalp to the amplitude range (volts) of the analog-to-digital (AD) converter. The smallest amplitude steps that can be sampled determine the resolution of the A/D converter. This is calculated by dividing the voltage range of the AD converter by 2 to the power of the number of bits of the AID converter. For example, an A/D converter with a range of 1:5 V with 12-bit resolution can resolve samples as small as 1:2.4 μV. Appropriate matching of amplification and AD converter sensitivity permits resolution of the smallest signal while preventing clipping of the largest signal amplitudes. The bandwidth of the filters and the rate of digitization determine the frequency components of the EEG and evoked response. The filter bandwidth is adjusted to insure that frequency components of interest are passed, while other frequencies outside the band of interest that may represent potential artifacts, such as aliasing are rejected. A filter's characteristics are determined by the rate of amplitude decrease of frequencies at the bandwidth's upper and lower edges. Proper digital representation of the analog signal depends on the rate of data sampling, which is governed by the Nyquist theorem that states that data sampling should be at least twice the highest frequency of interest. In addition to the information available from the spontaneous electrical activity of the EEG, the brain's electrical response to sensory stimulation can contribute data as to the status of cortical and subcortical regions activated by sensory input. Due to the relatively small amplitude of a stimulus-evoked potential as compared to the spontaneous EEG potentials, the technique of signal averaging is used to enhance the stimulus-evoked response. Stimulus averaging takes advantage of the fact that the brain's electrical response is time-locked to the onset of the stimulus and that the non-evoked background potentials are randomly distributed in time. Consequently, the average of multiple stimulus responses will result in the enhancement of the time-locked activity, while the averaged random background activity will approach zero. The result is an evoked response that consists of a number of discrete and replicable peaks that occur, depending upon the stimulus and recording parameters, at predicted latencies from the onset of stimulation. And finally, the spatial localization of maximum peak amplitudes has been associated with cortical generators in the primary sensory cortex.

RATIONALE FOR USE OF CEREBRAL MONITORING IN THE OR AND THE ICU

More than any other part of the entire organism, anesthetics and other centrally active agents affect the central nervous system profoundly. Because the CNS commonly is not monitored during anesthesia, episodes of malperfusion or hypoxia, or incidences of awareness during anesthesia, seldom are detected shortly within seconds after their beginning (Figure 1).

Although the various techniques such as computer tomography (CT), magnetic resonance imaging (MRI), magnet resonance tomography (MRT), Electro-Magnetic Tomography (EMT) from the EEG or the magnetencephalography (MEG) with a high resolution, or positron emission tomography (PET) are available for the clinician to gain further insight into cerebral function, methods to monitor routinely the CNS cannot replace the EEG, which over time has changed considerably. Despite the fact that the target organ of all anesthetics is the CNS, the different planes of anesthesia are commonly evaluated by means of an reaction of the cardiovascular system and the indices of an insufficient level of analgesia are determined by an increase in heart rate and blood pressure, an increase in

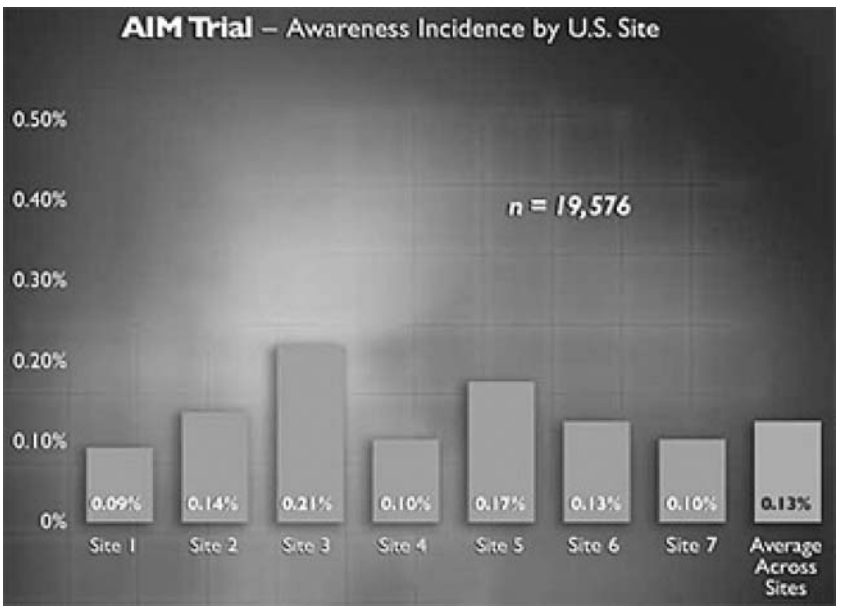


Fig. 1. The overall awareness incidence according to a study in different institutions over the entire US.

the respiratory rate or movements of the limbs. However, with the widespread use of muscular blocking agents, the administration of β-blockers or ACE inhibitors for therapy of high blood pressure, some of these simple signs to determine a sufficient level of anesthesia are not available any more. Also, unsuspected level of awareness during total intravenous anesthesia (TIVA), which are associated with psychic stress, present an unsolved problem when cerebral monitoring is not an integrated part in the anesthetic procedure [1, 2].

Apart from these drawbacks, the anesthetic state by itself limits the ability of the anesthesiologist and the surgeon to evaluate those parts of the CNS, which may undergo serious injuries, and which may occur during neurosurgical, spinal, cardiovascular or orthopedic interventions. Thus, the electroencephalographic activity of the cerebral cortex and evaluation of the integrity of nervous structures is possible using a monitor of an organ, which not only is the target of anesthetic agents but also at the same time is most sensitive to ischemic and hypoxic events. Therefore, the use of the EEG and the evoked potential is to determine the depth of anesthesia and detect episodes of ischemia respectively.

In the intensive care unit (ICU) patients undergoing sedation present a pharmacologically depressed state with unconsciousness which hampers the neurological assessment in situations when information about the functional integrity of neuronal structures is most needed to guide the treatment or predict the outcome. In order to circumvent all these drawbacks in today's anesthesia and intensive management, electrophysiological monitoring of the nervous system has gaining widespread use since the 1980s [3–6].

Application of techniques for noninvasive monitoring of CNS activity and functional integrity of neuronal structures in either the operating room as well as the critical care unit used to be very complex and expensive. Thus, many centers engaged in such activities provided them with additional information in order to prevent the patient from neurological injury [7–9]. Due to the rapid development in computer technology, and computer-aided data acquisition and comprehension in the past decade, electrophysiological monitoring is gaining new interest for the clinician. This is partly due to the fact that neuromonitoring enables the clinician to gain insight into the mode and the site of action of various centrally active agents and partly due to computerized simplification of data display and comprehension, which enables fast interpretation of central nervous effects. And lastly, computer application has simplified neuromonitoring to such a degree that little additional training is necessary to sufficiently derive electrophysiological data from patients under anesthesia and read the comprehensive data in a graph with sufficient ease, which are computed by microprocessors and displayed on a screen.

Since computers and microprocessors are much faster in data acquisition, transformation, and comprehension, they are much more reliable and also suitable to take over a good deal of work in electrophysiological monitoring. For instance, an experienced electroencephalographer would

be needed to examine EEG readings which, when they are recorded, come into different shapes of waves while extracting certain features from these tracings. He would process the EEG waves in his mind using the database to operate with, compare the data with past information and finally produce a result. Computer processing as it is used now, uses a similar approach. While examining the entire tracing, specific features are extracted. Just what features are extracted and how well they are presented determines the usefulness of computer-processed monitoring of central nervous activity. Thus, in the past, various concepts in data processing and evaluation have been developed, some of which have broadened our view of central nervous system activity and have given us additional insight into the reaction of the CNS to therapeutic maneuvers. Some of these concepts have lived a short life as processing was not sophisticated enough and the display too complicated to gain additional information [10, 11].

During the development of EEG recording, interest among clinicians was characterized by burst of enthusiasm, which however, was followed by periods of little or no interest. While use of electrophysiology in neurological investigations developed rapidly and had maintained its importance as a diagnostic tool so that virtually every large size hospital has its own EEG department, the anesthesiologist and those clinicians working in the intensive care unit, however, have not taken this up. Confusion has spread about the use and the possible advantage of neurophysiologic monitoring in the OR and/or the ICU. The cause of this confusion stems largely from the complicated technique and the size of the device necessary to run an EEG analysis and the successful integration of cerebral monitoring in the daily activities. Although the same signal may be under investigation, there are distinct differences in regard to its interpretation. Because the EEG signal is very different, when a focus of abnormal electrical activity is undergoing investigation, or when a normal person shows EEG changes which are due to the action of an anesthetic agent or are related to hypoxemia [9, 12–16]. And although in both cases the signal comes from the same electrical activity of the CNS, its interpretation, however, is very different. For the anesthesiologist or the intensive care therapist who wish to make intelligent use of the information provided by the electrophysiological monitor, the first requirement is to be able to recognize the standard signal associated with normal physiological changes. Therefore, a rational assessment from neuromonitoring can only be made in the light of the underlying disease, the use of an anesthetic, or the underlying pathology in a comatose patient. Such basic information is necessary when interpreting the results of computerized EEG and evoked potential monitoring which eventually will result in a decision making in the next therapeutic step.

WHY MONITOR THE ELECTROENCEPHALOGRAM (EEG)

Until the past 10 years EEG monitoring outside the diagnostic laboratory has met limited use despite its clear role in areas such as anesthesia, head trauma, and intensive care treatment. Primarily, there are three reasons why the clinician resented the fact of using the electroencephalogram in his daily work:

1. The size and the complexity of the conventional EEG equipment,
2. The laborious reading of bulky EEG tracings,
3. The need for a trained physician to run the EEG machine [17].

Because of the advantages in electronic technology, however, these obstacles have been overcome and presently there is a synthesis of the most significant aspects in EEG recording even at the cost of sacrificing details resulting in a quantification of EEG waves.

Quantified electrophysiology refers to the computer-based acquisition, display, storage, and analysis of EEG or stimulus, event-related response in the evoked potential (EP). The data can be evaluated in the time domain or converted to the frequency domain. The latter permits analysis of the EEG and EP based upon the frequency components of the signal. The spatial distribution of the dependent variables are frequently presented as two-dimensional topographic color maps. Quantified eleetrophysiology has been advocated as an adjunct to traditional EEG and EP recordings. It offers a method to quantify aspects of the EEG that have been routinely evaluated qualitatively. The unique and promising advantage of quantified electrophysiology is the ability to quantify aspects of the EEG and the evoked potential that are not observable from visual inspection of the time-domain record and that may convey information concerning cerebral function, correlates of cognitive activity, neurophysiologic mechanisms, spatial localization of cortical generators, and diagnostic classification. The data lends to statistical analysis for evaluating objectively within-subject changes during experimental manipulation or individual comparisons to age-adjusted normative databases. The emergence of quantified electrophysiology has been driven, mostly by the recent advances in microprocessor technology. The hardware and software requirements for signal acquisition, display, analysis, and storage that were once only available on expensive mainframe systems have been implemented in low-cost personal computers. This has resulted in an increase in the accessibility of this technology and an expansion of the clinical and experimental applications of quantified electrophysiology and clinical diagnostic findings. Along with the proliferation of this

technology, controversies concerning various aspects of the methodology and its application used to exist, however, in the meantime have dwindled. These issues relate to data acquisition techniques, the physiological significance of the variables derived from spectral analysis, the spatial relationship between scalp potentials and cortical generators, the limitations of topographie mapping, and the appropriate statistical analysis of the multiple variables derived from quantitative electrophysiology.

The present book will not only review the methodology and applications of quantified electrophysiology, but techniques of data acquisition will be presented from the perspective of their effects on frequency analysis and its practical use in the clinical environment.

Among the various microprocessor-related procedures used to computerize the native EEG reading, the transformation from a time to a frequency domain now offers a comprehensive picture of the raw EEG activity and of the distribution of the dominant frequencies and their revolution in time. Utilizing this method, it is now possible to calculate in real time the spectral power amounts of the EEG, which are useful in a number of clinical settings [9]:

1. They provide continuous information of the onset, depth, and the duration of an anesthetic on neuronal structures.
2. They indicate arousal during anesthesia, which could have been induced by the surgical stimulus or by an insufficient concentration of the anesthetic.
3. They anticipate the time of awakening and of recovery from anesthesia.
4. They assess total recovery from anesthesia.
5. They confirm satisfactory cerebral perfusion during special types of operation such as cardiopulmonary by-pass, carotid endarterectomy, and during deliberate hypotension.
6. They provide continuous and objective record of sufficient cerebral oxygenation.
7. They immediately are able to assess the effects of hypoperfusion and/or hypoxemia on cortical structures and rapidly demonstrate the benefits of corrective measurements.

As the EEG is a minute, brain-generated voltage differential between two arbitrary sites on the scalp, the potential changes represent activity of only a small portion of the brain. It can be estimated that the actual EEG represents a sampling from no more than one third of all brain cells. As to the site of origin of cortical potential changes, it appears that the post-synaptic potential changes of cortical pyramidal or Betz cells (Figure 2) play an important part in generating the electrical changes [18].

Experiments have demonstrated that medial and intrathalamic nuclei play a central role as cortical pacemakers. The rhythmic activity of discrete cell groups in these specific thalamic nuclei synchronizes the activity of corresponding cortical projection areas by every mm^2. Although the cortical cells by themselves are able to induce rhythmic activity of their own, the subcortical pacemaker is a prerequisite for inducing spindling of EEG waves [19, 20] (Figure 3).

THE NEUROLOGICAL APPROACH TO EEG INTERPRETATION

In 1926 the famous German psychiatrist Hans Berger (Figure 4) was the first to monitor the minute potential changes from the cerebral cortex in man. Although using a cumbersome galvanometer, he was already able to differentiate various stages within these potential changes, which he attributed to dissimilar physiological states. In his publication on the "Elektenkephalogramm" of man he already had used non-polarized electrodes placed on the scalp of patients noting a difference in architecture of waves when the patient opened or closed his eyes, or when he went to sleep. Even now his basic observations serve as a cornerstone when native EEG waves are analyzed in a classical approach.

Berger already had observed that electrical activity of the cortex are evident in states such as sleep, wakefulness, and arousal while abnormal electrical activity can signal epilepsy or mental illness (Figure 5).

When evaluating patterns of the native EEG, classically they are recognized by analyzing the signal with respect to its frequency, amplitude, and asymmetry.

– *Frequency* is the measurement of the number of times a respective wave reoccurs in one second interval. Most of the EEG activity occurs between 1–30 cycles per second, which equals the dimension in Hertz (Hz). The frequencies of EEG waves traditionally have been divided into four standard bands (Figure 6):

   a. The delta band = 0.5–3 Hz
   b. The theta band = 4–7 Hz
   c. The alpha band = 8–12 Hz
   d. The beta band = 13–30 Hz

Each individual EEG pattern is distinctive, but according to international terminology, four characteristic patterns of electrical activity can be attributed to different physiological stages (Figure 7):

Alpha waves with a frequency of 8–13 Hz are associated with relaxed wakefulness. Beta waves with a frequency of 13–30 Hz are seen in individuals who are awake, alert, with eyes open, and who may be concentrating on something.

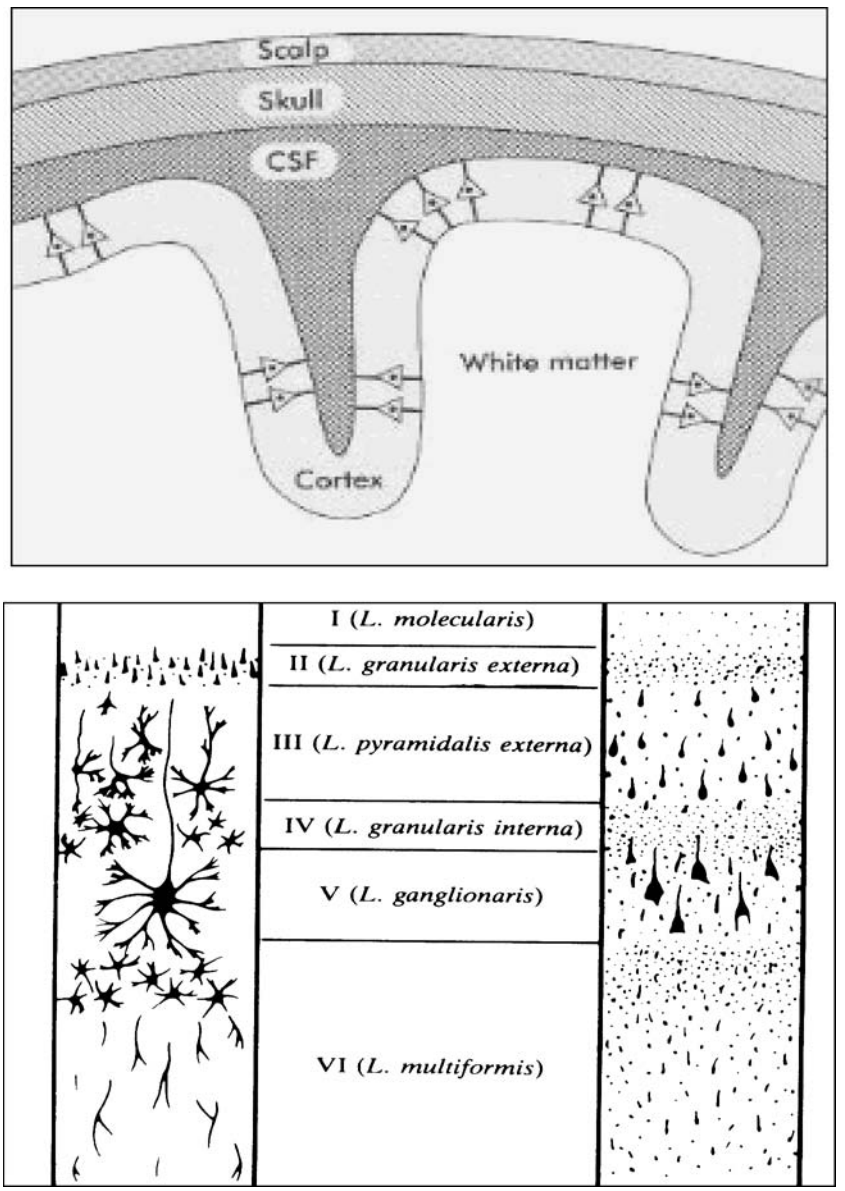


Fig. 2. Different cortical layers and their nerve cells which are involved in the generation of minute electrical potential changes.

Delta waves with a frequency of 0.5–4 Hz are associated with sleep in adults but are also seen in infants. Their abnormal appearance in the awake adult can be indicative a brain lesion.

Theta waves with a frequency of 4–7 Hz are also seen in the sleeping adult and in children. Their abnormal appearance in adults has been seen in certain psychiatric disorders.

– *Amplitude* refers to the height of EEG waves as measured in microvolt (μV) and categorized rather loosely in the following subunits:
  a Low amplitudes = less than 20 μV
  b Medium amplitudes = 20–50 μV
  c High amplitudes = more than 50 μV

– *Symmetry* generally refers to the EEG of both hemispheres of the cortex. For instance anesthetic agents usually affect both hemispheres symmetrically, while a reduction of blood flow to one side of the brain as pathologically induced carotid stenosis, may result in asymmetry.

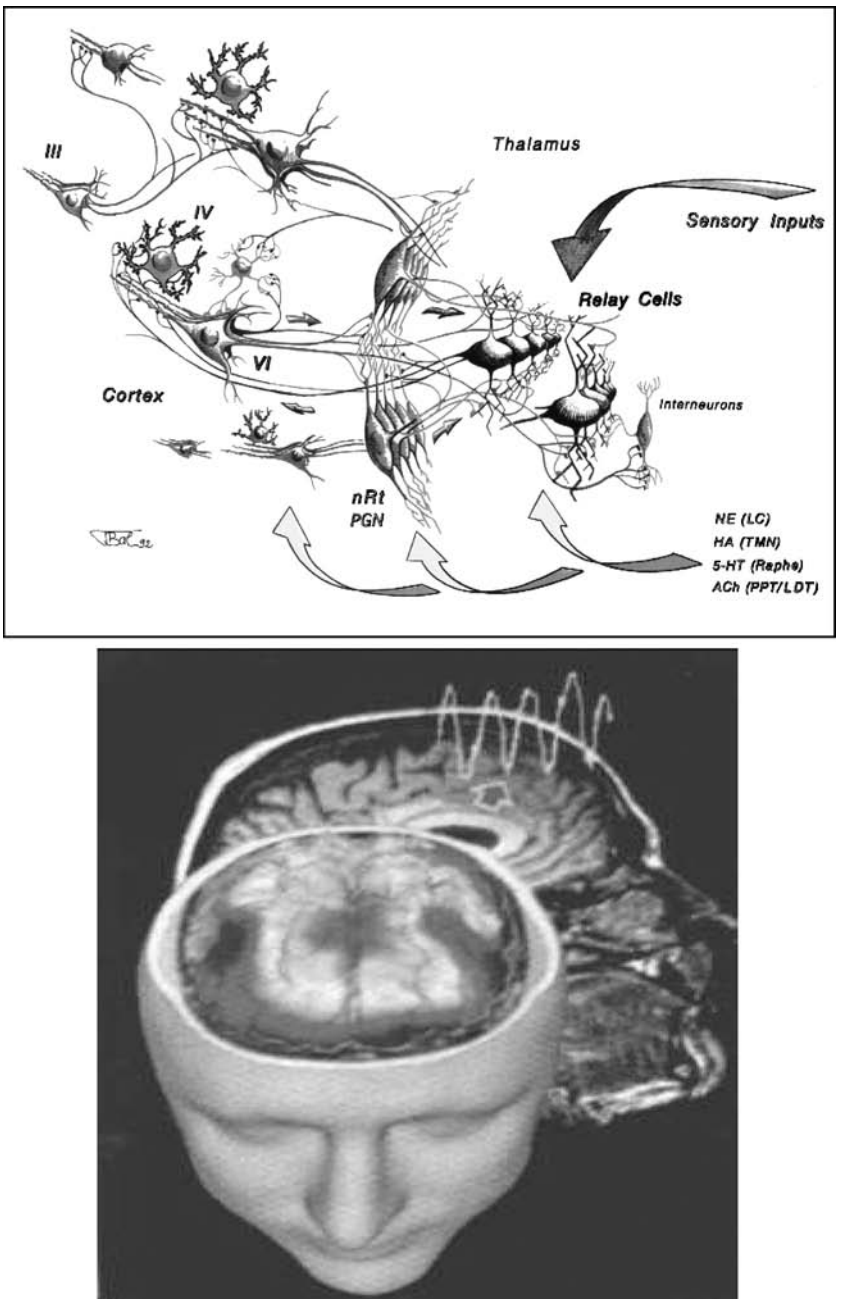


Fig. 3. The thalamic pacemaker for cortical activities as they are recorded in the EEG.

BASICS OF EEG MONITORING

Overview of electrode technology in EEG monitoring

The EEG (electroencephalographic) measurement and recording system, although analogous to the method used for ECG (electrocardiographic) measurement, varies in that the EEG machine:

1. Has additional flexibility,
2. Is more susceptible to artifacts since the potential changes of the superficial, cortical layers are amplified by a factor of 100,
3. Measures potential changes in microvolt (μV) while those of the ECG are in millivolt (mV).

Electrical signals re generated by a number of organs in the human body. In particular, signals generated by the

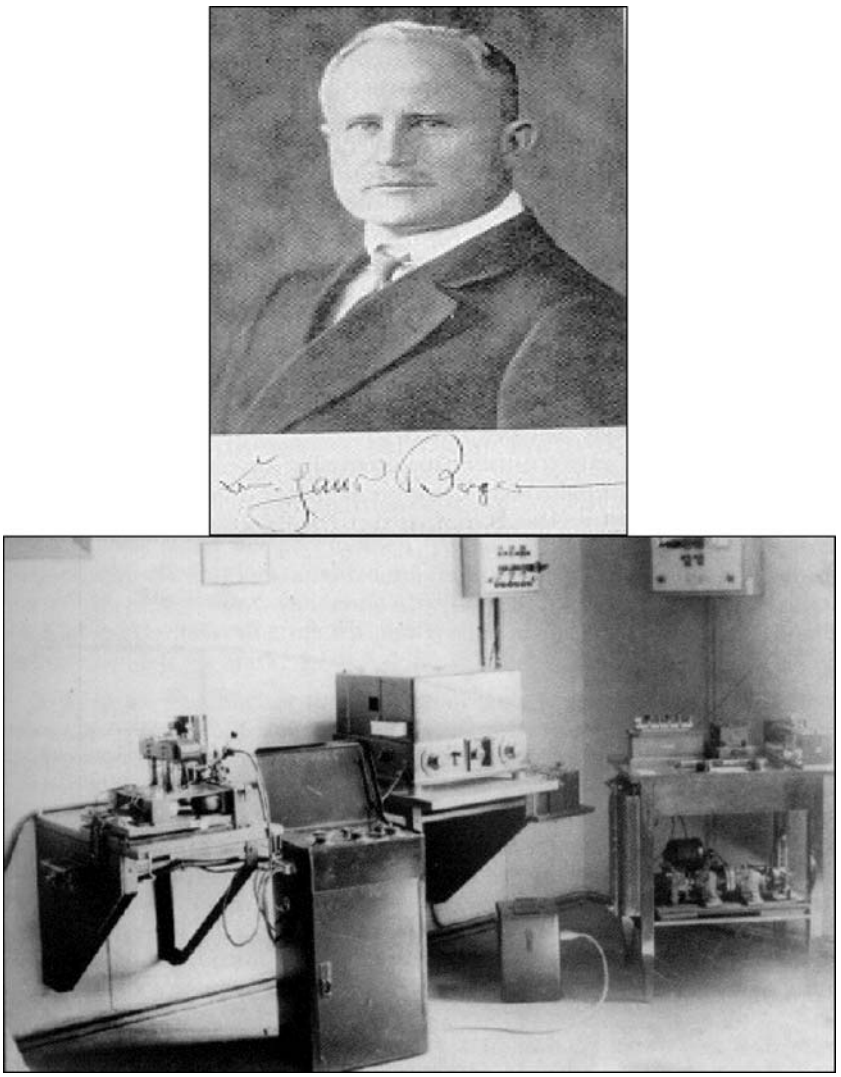


Fig. 4. Picture of the German psychiatrist Hans Berger and his EEG lab in Jena/Germany where he was the first to differentiate electrical potential changes in man in 1929.

heart and the brain are frequently used to assess the state of a patient. While the electrocardiogram (ECG) is indicative of cardiac function and gives a time-portrait of the electrical behavior of the heart (Figure 8), the electroencephalogram (EEG) can reveal brain states including epileptic focal activity, consciousness patterns generated in sleep, detect neurological deficits, direct the attention to changes in the metabolic state, and the effects of anesthetics.

Since they originate from neural tissue in the brain, especially of the superficial cortical layers, and they present minute potential changes, impedance of the sensors, which pick up this activity, is of utmost importance.

WHAT IS IMPEDANCE IN REGARD TO ELECTRODES?

Impedance is the electrical resistance in a varying current flow, such as in the current flow associated with a bio-potential signal propagating through the patient's skin. While impedance plays a critical role in the quality of signals for ECG waveforms, the low voltage level of the EEG waveforms makes the need for low impedance even more critical. To better appreciate the value of low impedance in EEG monitoring, one must first have a basic understanding of the impact of impedance levels on the native EEG.

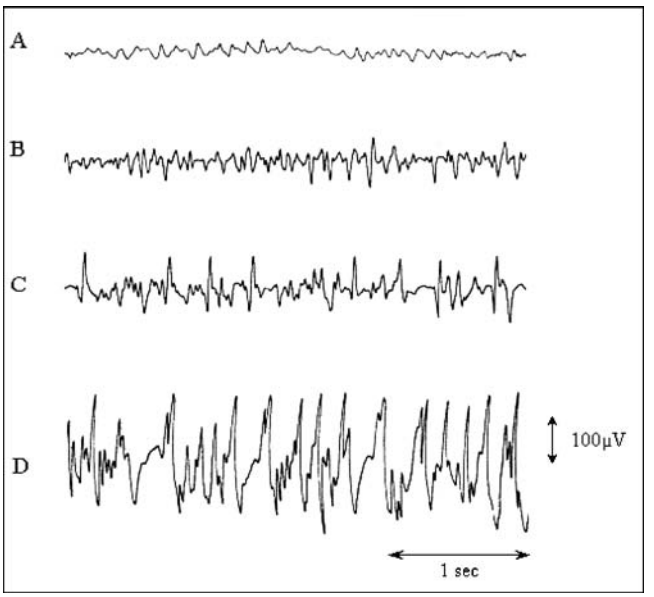


Fig. 5. Different electroencephalographic patterns depicting the awake, normal state (A–B) and a state with epileptic discharges (C–D).

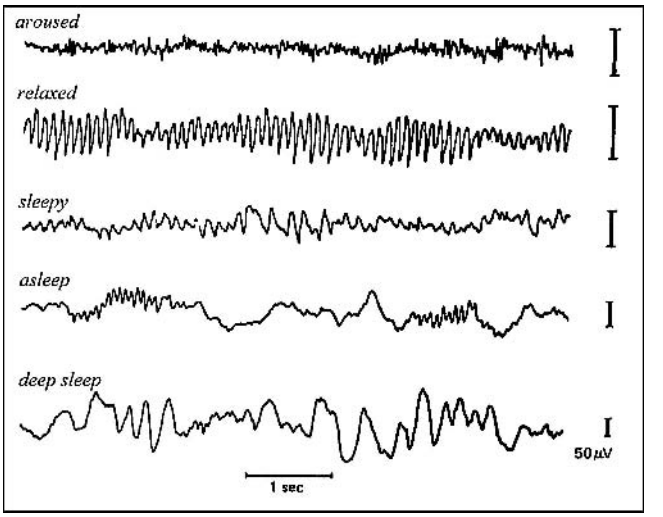


Fig. 7. Representative examples of the different classical EEG-frequencies in sleep. Each band is associated with a certain physiological state where beta is referred to as being awake and attentive, alpha dominance is found in a relaxed and drowsy state, while theta- and delta-band reflect different stages of sleep or sometimes indicate a pathology.

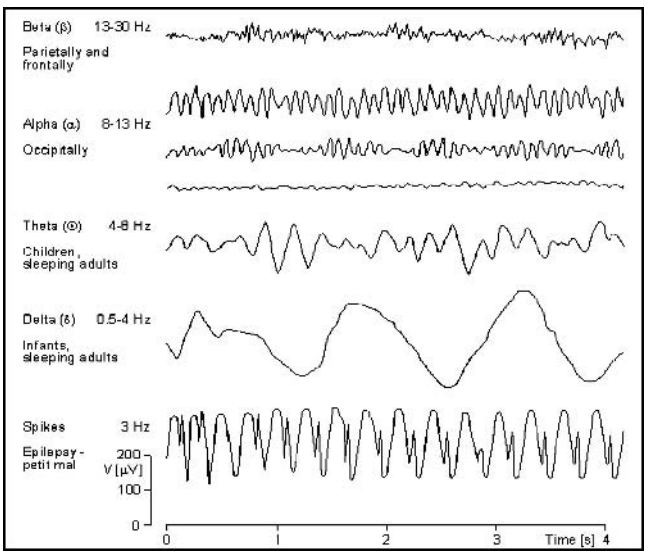


Fig. 6. Characteristically patterns of the different EEG waves related to different physiological stages.

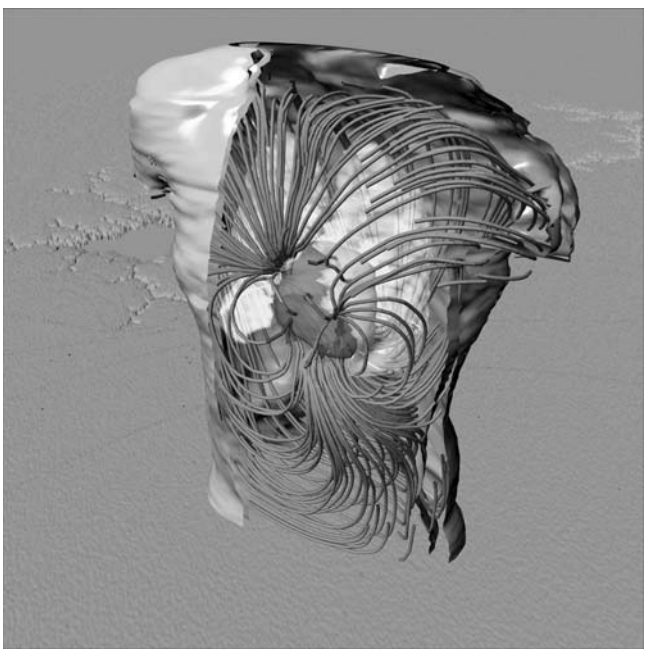


Fig. 8. Principle of the number of vectors in electrical current flow of the myocardium, which enables the recording of the ECG with potential changes in millivolt.

WHY IS LOW ELECTRODE/SKIN IMPEDANCE IMPORTANT IN EEG MONITORING?

Maintaining low electrode/skin impedance levels will reduce the noise in the EEG systems in two important areas:

1. *Thermal noise.* One of the contributors to noise in the EEG system is the thermal noise, also called Johnson noise [21]. Thermal noise is caused by random fluctua-

tions of the molecules within a conductor. The size (or voltage) of this noise is directly related to the amount of impedance exhibited by the conductor. For example, if two electrodes (conductors) exhibit a combined impedance level of 20,000 ohms in a 100 Hz bandwidth, 0.18 microvolt of thermal noise will be generated. Given that the amplitude of the EEG signal ranges from 0.25 microvolt up to about 100 microvolt, it is apparent that the presence of 0.18 microvolt of noise could significantly affect recordings of the lower amplitude EEG signals. Therefore, it is important to maintain the electrode-skin impedance as low as possible in order to achieve the highest possible signal (EEG)-to-noise ratio.

2. *Common mode signal rejection*. Differential amplifiers are used in EEG systems to obtain the signal. Hence, the displayed EEG signal is the difference between a pair of electrodes. Signals that are common to both electrodes should not be displayed in the EEG. This is called Common Mode Rejection (CMR). Many types of artifact signals (such as 60 Hz power line noise, ECG, etc.) will appear equally in (common to) both electrodes, and will, be rejected by the EEG system.

However, if the impedance of the electrode pair is imbalanced (unequal) the common artifact signal will appear slightly different at the amplifier inputs to the EEG system. If this occurs, the artifacts will not be completely rejected and will be processed by the EEG system as though they are actual EEG. An example of this is shown in Figure 9. Two baseline EEG signals were recorded simultaneously. Channel 1 was recorded with low and balanced impedance levels of 2,400 and 3,100 ohms. Channel 2 was recorded with an electrode pair that exhibited imbalanced impedance levels of 2,400 and 50,000 ohms. Motion artifact (common to both electrodes in each channel) affected Channel 2 resulting in slow "delta-like" waves that could affect the interpretation of the signal. The best way to ensure that the impedances are balanced and hence, more resistant to artifact, is to make each of them as low as possible.

The importance of a low impedance between the electrode and the underlying skin is underlined in the following picture where contrary to EEG recording with a low impedance (>5 KOhm), high impedance results in the pick up of electrical interference from the ECG (Figure 9).

In this respect, the recording instrumentation is of utmost importance as poor quality of recording electrodes result in a poor signal, many artifacts, resulting in difficulties of interpretation. For the sake of accuracy it is always necessary to use non-depolarisable electrodes, which are capable of recording EEG frequencies over a wide band pass.

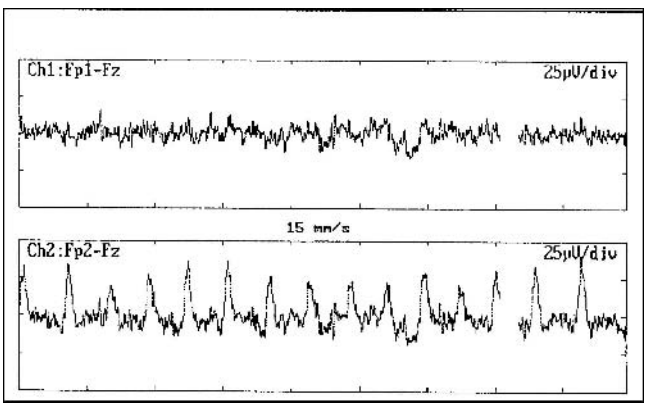
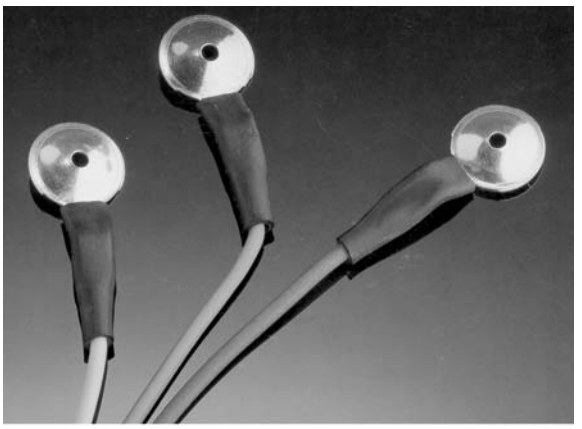


Fig. 9. Representative example of two original traces of EEG recording with low (upper trace) and high (lower trace) impedance using a paper speed of 15 mm/s.

THE TYPE OF ELECTRODES FOR RECORDING

There are three types of electrodes, which generally can be used in recording EEG waves in the OR and/or the ICU (Figures 10–14):

1. Specially prepared silver or gold cup electrodes with a diameter of one cm coated with silver chloride (AgCl) or gold. They are fixed to the scalp with *collodium* or an adhesive plaster (Figure 10), and are filled with saline gel similar to the one used for ECG recording or in sonography. The main purpose of this gel is to lower impedance.
2. Sterilized stainless steel or platinum subdermal needle electrodes. Their main advantage is that they can be applied quickly to the patient (Figure 11). However, they have high impedance, which makes them more susceptible to electrostatic interference from other electrical appliances located nearby the recording site of the patient.
3. In addition, so-called corkscrew electrodes are available, which results in a more secure position when applied to the scalp (Figure 12).
4. Disposable and pre-gelled Ag/AgCl-ECG pad electrodes with a 30 × 22 mm diameter as they are used in recording of the electrocardiogram (Figure 13). They are applied on areas with no hair where the application site has been cleaned with alcohol for increase of adhesion and the skin is shared for the reduction of skin resistance.
5. *Scalp pad electrodes*: This type of electrode is usually applied to patients outside the OR or the ICU because at least 16 leads are used, which takes some time for proper application and fixation using a rubber made head set (Figure 14).



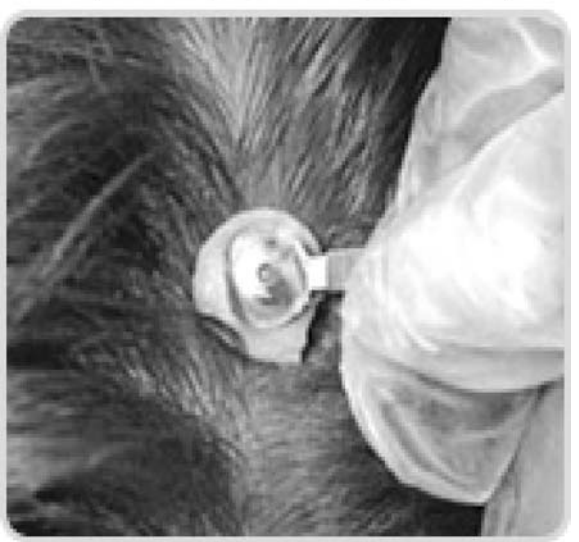


Fig. 10. The silver or gold cup electrode being applied to the scalp with an adhesive plaster.

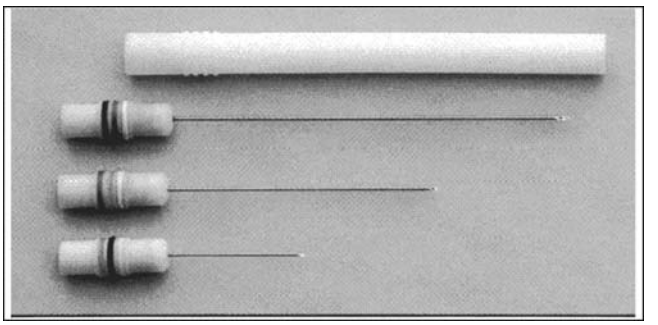


Fig. 11. Subdermal needle electrodes as they are used for EEG measurement.

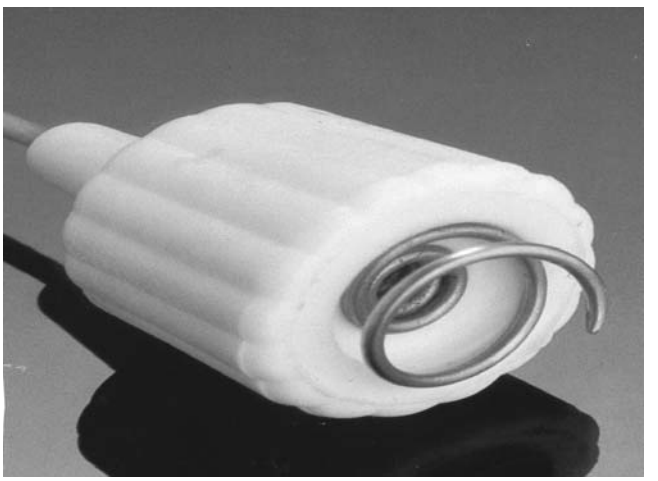


Fig. 12. The corkscrew type electrode, which is also made out of stainless steel.

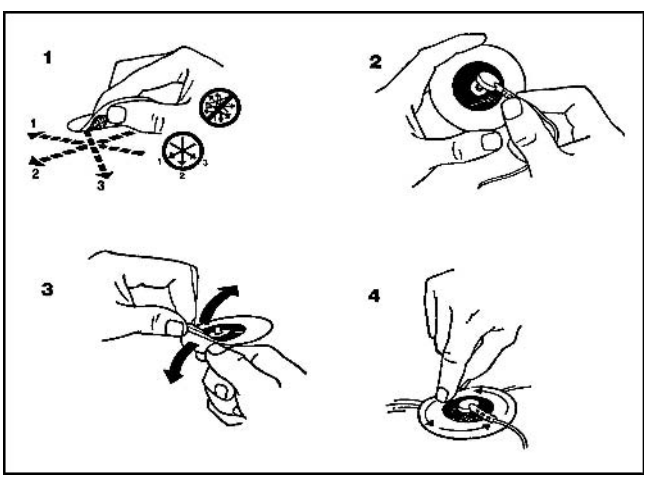


Fig. 13. Preparation of skin site and application of Ag/AgCl skin mini pad electrode for EEG recording.

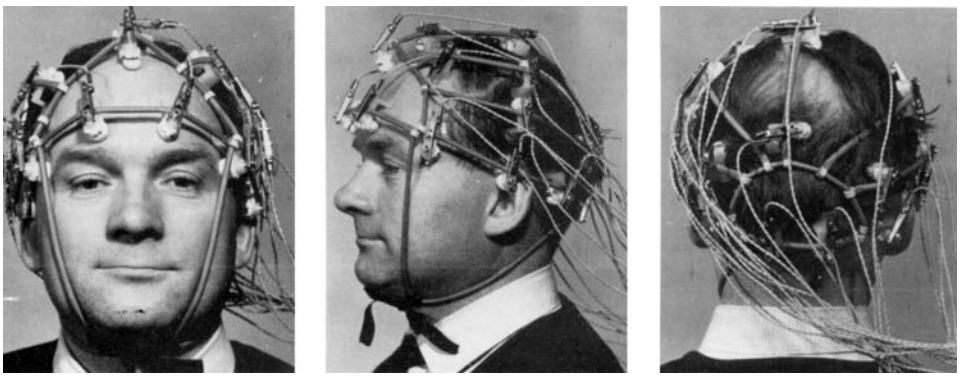


Fig. 14. Front, side and back view of scalp electrodes being held in place by a rubber head set.

Such scalp pad electrodes are used, for instance, in neurology in order to identify the focus of epilepsy, check for a possible tumor, or differentiate the cause of a chronic headache.

FACTORS AFFECTING ELECTRODE IMPEDANCE

Empirical studies have shown that the major contributor to the impedance level of a pair of skin contact electrodes is the skin itself, with the greatest impedance being found in the outermost layer of skin. This outer layer, the epidermis, consists of dead cells, which are rubbed off as you move, wash or abrade the skin. The outer layer of dead cells causes the electrode/skin impedance to be "very high" (typically 30,000 to 90,000 Ohms to as high as 1,000,000 ohms).

The second factor to consider is surface area. Large diameter disks have more surface area than smaller disks and for this reason have lower impedance. This is why needle electrodes, which have a small surface area may show a relatively high impedance even though they penetrate the skin. However, simply increasing the size of the electrode contact area alone would not reliably bring the impedance level below the desired 5,000 ohm range [22]. Finally, there are some impedance-related artifacts that can arise from electrode drift on the skin, bunching and folding of skin, and puckering of the epidermis (from prolonged exposure to moisture). These artifacts can be partially mitigated through the use of an appropriate adhesive.

CURRENT METHODS USED TO LOWER IMPEDANCE

To lower impedance, it is necessary to penetrate the outer layer of the skin. The most commonly used method is to abrade the skin by applying an abrasive solution to a cotton swab and rubbing the skin in a circular motion 10–20 times or until the skin is pink. One of the disadvantages of this method is the possibility of breaking the skin, which may result in bleeding or soreness. Using this method, it is also common to inadequately prepare the skin necessitating reapplication of the electrodes. Also, this technique can be time-consuming and unreliable.

The Zipprep™ electrode technology utilizes a simple, yet elegant method for lowering the impedance of the electrical contact with the skin. The so-called Zipprep™ electrode is a teardrop shaped, disposable pre-gelled electrode that is applied directly to the skin of the patient to record electro-physiological signals. The teardrop shape is made from a dense blue polymer foam material with a pressure sensitive adhesive on the underside. Within the teardrop shape, the electrode contains an electrically conducting Silver/Silver Chloride (Ag/AgCl) flat element, which connects through the overall electrode structure to a nickel-plated brass snap stud located on the top of the electrode. A layer of liquid hydrogel is deposited on the under-surface of the snap element. Immersed in this liquid hydrogel is a polymer disk containing multiple small flexile tines. The liquid hydrogel material surrounds the tines of this disk. A foamed polymer material retaining surrounds this assembly of elements.

The Zipprep™ disposable electrode achieves low impedance levels without the need for additional prepping steps that involve abrading or removing the outer dead-cell layer. When the electrode is applied to the epidermis of the patient, the disk is gently pressed onto the skin. The polymer tines part the outer layer of dead cells and allow the hydrogel to reach the next layer of the epidermis. As discussed earlier, the outer layer of skin cells represents a high impedance barrier to signal flow. By parting this outer layer, the hydrogel can come into contact with the next layer of cells in the epidermis, which is more conductive. A low impedance contact with the skin is achieved, Ag/AgCl ECG electrode. This set of Ag/AgCl sensors in a sophisticated electrode system was specifically designed to work with a selective EEG machine such as the BIS, the

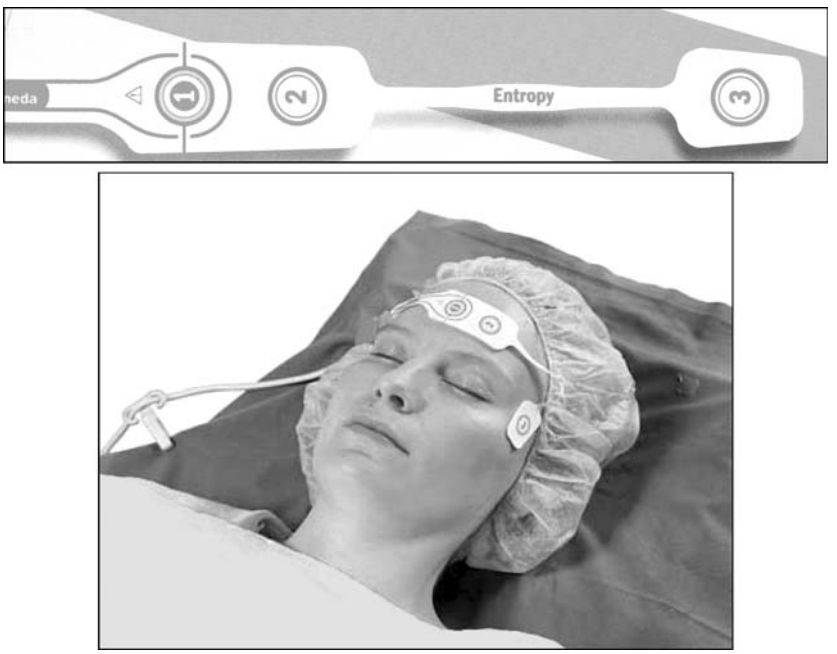


Fig. 15. Representative examples of the new electrode type of the three-in-one technique, where three electrodes are located in a flat element, which connects through the overall electrode structure to a nickel-plated brass snap stud located on the top of the electrode, which is placed on the fronto-temporal side of the head.

Entropy and the PSA 4000. A family of sensors [3] tailored to different clinical applications or different patient sizes is available (Figure 15). After minimal skin preparation, the single-use sensor is placed on the forehead of the patient with a specific orientation over either the left or right hemisphere. Advanced electrode technology results in low impedance values, allowing reliable capture of raw EEG data and increasing the fidelity of the EEG signal.

The purpose of the electrodes is to provide an efficient interface between the scalp potential and the insulated amplifier. The key element to *electrode efficiency* is to minimize the impedance to electrical current flow. Excessive electrode impedance leads to a decreased EEG signal and a frequency-dependant distortion of EEG-waves. Therefore, meticulous care must be taken when applying the electrodes as they present the prime source of artifacts, electrical interference and a bad recoding signal. It is because of this importance that every EEG-device continuously measures the impedance, which can be viewed on a screen. The two major sources of excessive impedance, which is measured in Ohm (Ω), are the stratum corneum, the upper layer of the skin, and the skin-electrode interface. Since the upper layer of the skin mainly consists of horn cells, which act like isolators, a high resistance is likely not to pick up the native EEG- waves. This resistance easily can be reduced by abrading the skin with an abrasive gel (e.g. Omniprep^{TM}). Therefore, when using a cup electrode, using a sufficient area of contact on the skin, and applying enough conductive gel, between skin and the dome of the electrode, the skin-to-electrode contact is increased. Normal electrode impedance should be <5000 Ohm or $<5\,k\Omega$. When using the cup electrode, it is attached to the skin by a layer of collodion around the rim, while the dome later is filled with sufficient conductive gel. Since collodion provides a more secure and permanent seal around the cup electrode than conductive paste, it generally is advocated for use in the OR and the ICU.

The following specifications have to be fulfilled in order to facilitate recording of the EEG or the evoked potential in the clinical environment:

1. Low impedance recording ($<5\,K\Omega$) with a small disposable electrode to maximize signal input, which will provide an accurate display of cerebral activity.
2. A simple and fast technique for electrode application, which reduces the need for a specialized technical skill, resulting in an increase in acceptance of clinicians who are willing to use cerebral monitoring in the OR and the ICU.
3. Specify areas of electrode placement in order to be able to compare signals of one patient taken at different times. Electrode placement on the scalp generally is done using the 10/20-system using different anatomical landmarks on the scull for identical positioning.

ELECTRODE PLACEMENT IN EEG MONITORING

Standard neurological practice requires a precise placement of electrodes in relation to anatomical landmarks of the skull. The internationally accepted system for electrode placement is the 10/20-system (Figure 16). The international 10/20-system for standardized placement of electrodes has been developed by the international federation of *Societies for Electroencephalography and Clinical Neurophysiology* to permit comparison of recordings obtained in different patients with differently size or shaped skulls [23]. The essence of the system is that the anterior-posterior measurement are based on distance between the nasion and the inion over the vortex of the middle bone, where fixed points are marked along this line at percentages of the 10% to 20% range of the nasion-inion distance. By calculating this range fixed points on the frontal pole (Fp), the central (C), the parietal (P), and the occipital point (O) are identified. Lateral measurements are based on the central, coronal plane from the preauricular point to the other. From here, the 10% to 20% range identify the temporal (T) points, where even numbers are used as subscripts of points over the right hemisphere and odd number identify those points over the left hemisphere. And lastly, midline electrodes have the subscript "z" which stands for zero (e.g. F_z, C_z, P_z).

TECHNICAL REQUIREMENTS FOR RECORDING A RELIABLE EEG SIGNAL (DIFFERENTIAL AMPLIFIER, FILTER-SETTING)

The EEG, which is detected on the scalp, is of low voltage and is almost overflown by physiological electrical potentials such as the ECG or the electromyogram (EMG). In addition, interference of other electrical appliances using AC current (alternating current between 50–60 Hz) can distort the EEG signal. To minimize interference of unrelated potentials, which may enter the EEG electrodes, a *differential amplifier* is used. It has two inputs, which represent the potentials at opposite polarities. This arrangement effectively cancels out both voltage signal common to both inputs, the *common mode rejection*, and amplifies only the voltage difference between the two inputs (Figure 17). In addition, electrical interference can be a major problem with intraoperative EEG monitoring since electrical signals from the brain are small and the operation room as well as the intensive care ward with its different electrically driven machinery (e.g. electrical infusion pump, respirator machine, ECG monitor etc.) present an electrically hostile environment for EEG recording. Also, electrode leads used for EEG measurement act as conductors, they at the same time can be considered as antennas. Therefore, the following points have to be kept in mind in order to obtain an artifact-free EEG recording in the OR and/or the ICU:

1. Keep the leads to the preamplifier as short as possible.
2. All electrodes should follow the same path to the preamplifier.
3. Reassure that the insulation of all electrodes is not broken at any point.
4. All electrodes should have the same length.
5. All electrodes should be made of the same material.

Also, in order to optimize electrical noise rejection during the recording period:

1. Strive for the lowest possible impedance between electrode and skin.
2. Try to have the same low impedance throughout the entire electrode montage.
3. Choose a montage of electrodes, which does not cross musculature.
4. Select an appropriate amplifier gain for the incoming signal.

However,

Electrocautery remains a problem during cerebral monitoring and any recording during this period should be interrupted

The preamplifier, due to its configuration, is able to:

– Amplify the difference between active pole and reference,
– Reject similarities between active pole and reference, the common mode rejection, which typically is around 100 db
– Points signal down at display when positive activity is at the active pole,
– Points signal up at display when positive activity is at the reference pole (Figure 17).

An additional technique to reduce electrical noise in the EEG takes advantage of the fact that the frequency of electrical noise generally is different from that of the ECG. Therefore, the use of frequency dependant *filter setting* balances prudently between a reduction of noise and a decrease in reliability of the true waveforms. As an example, in Figure 18, electrical noises, which contains a random mixture of various incoming signals is gray, whereas EEG waves contain only selected frequencies usually between 0.5–30 Hz (Figure 18).

The objective of filtering is to remove the noise, which does not overlap the signal, preventing it from entering the microprocessor for further analysis. The sharp edges, as shown in the Figure 18 present the low-cut and the high-cut site, where "noise" frequencies are blocked. The actual filter system, however, has a gradual slope; therefore

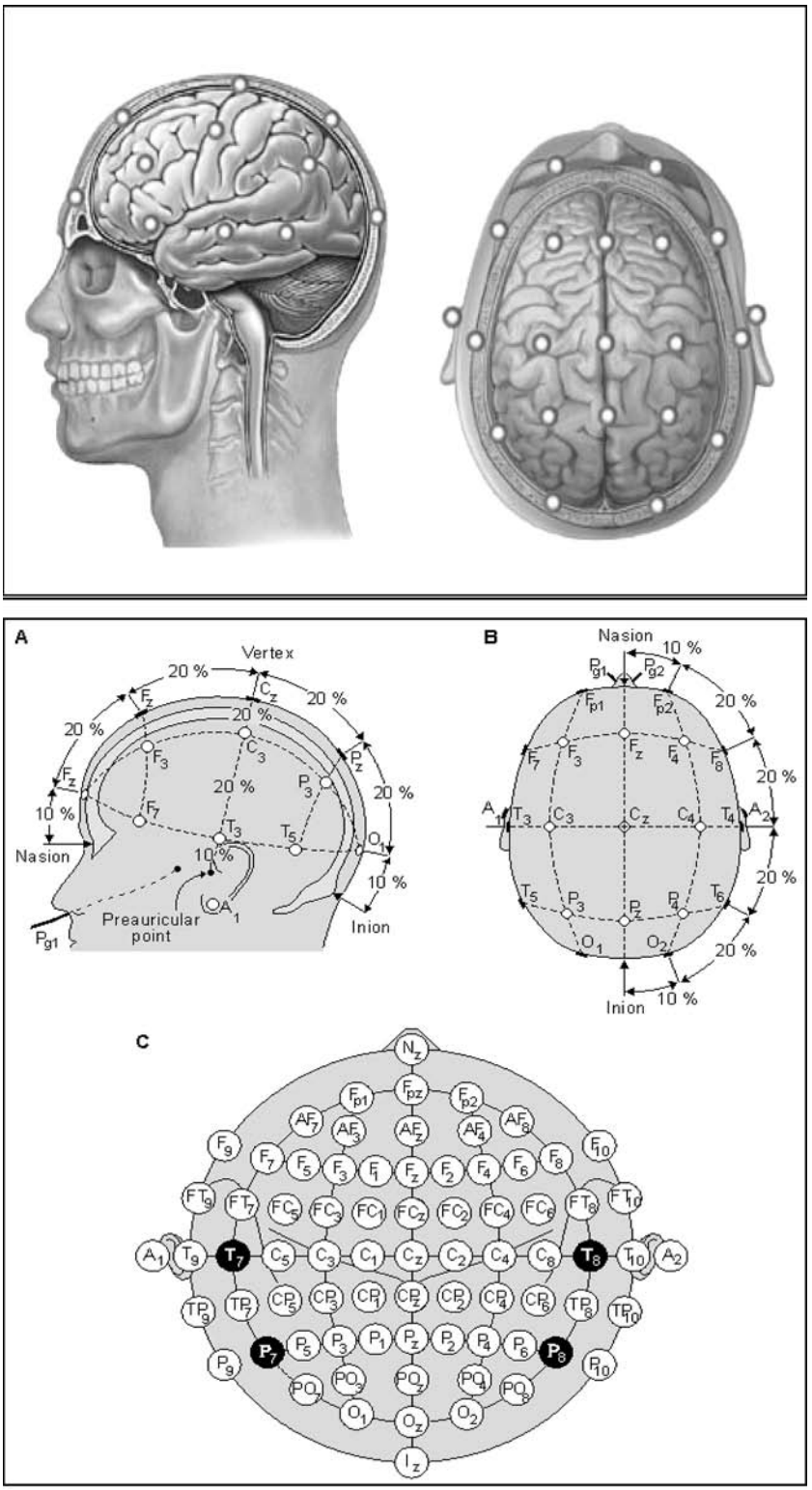


Fig. 16. The international ten/twenty-system for placement of electrodes on the scalp in regard to different anatomical landmarks of the skull. A: side view, B: top view, C: classical montage with 36 electrodes as used in epilepsy monitoring.

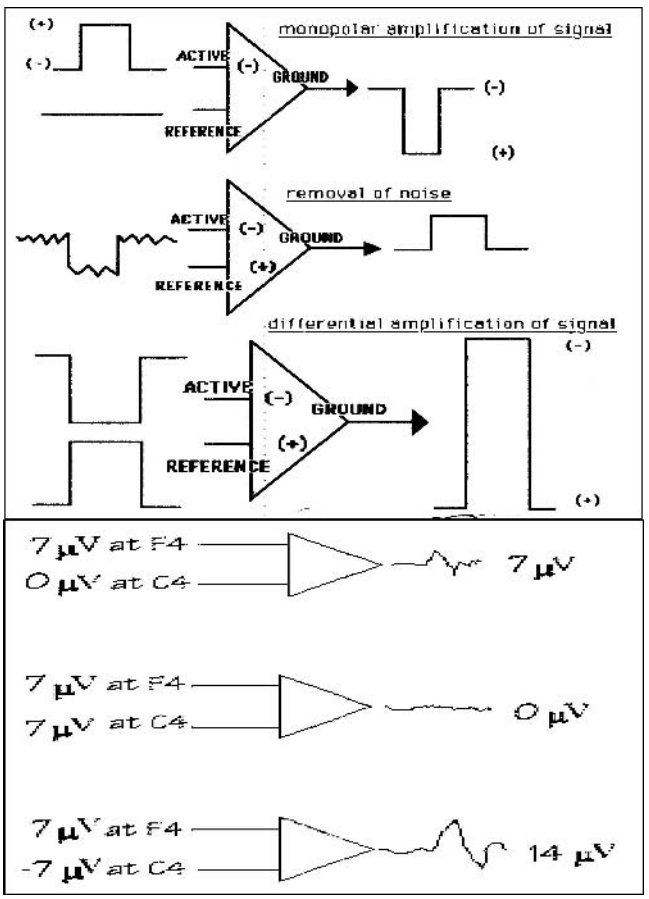


Fig. 17. Activity of the preamplifier during EEG measurement, which due to its configuration, is able to change the incoming signals.

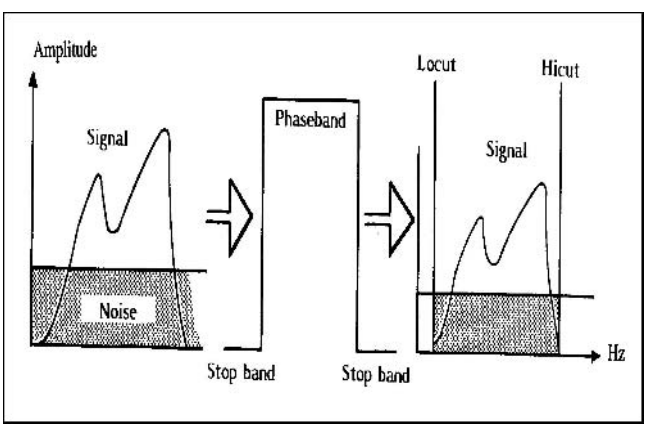


Fig. 18. Schematic presentation how electrical noise is filtered out during EEG recording.

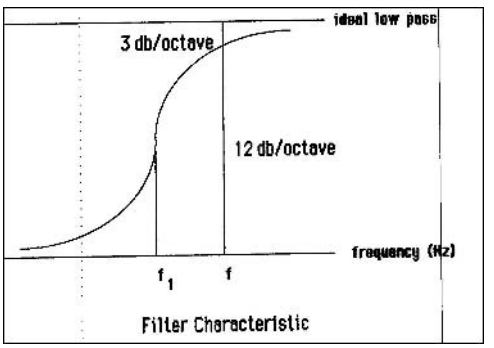


Fig. 19. The principle of filter settings to prevent electrical noise from entering the EEG machine for further analysis, considering only relevant EEG frequencies.

noise is not totally eliminated. For standard clinical EEG reading in the OR and the ICU filter setting usually is set at 0.5 (high pass filter) and 30 Hz (low pass filter). Commonly accepted, this band pass represents the best compromise for EEG reading in an environment, which is characterized by a concomitant increase in electrical noise (Figure 19).

THE RECORDING PROCEDURE

A combination of electrodes used for cerebral monitoring is referred to as an *electrode montage*. The montage chosen for a given situation depends on what area of the cortex is to be examined and what information is being sought. Basically, there are 3 types of montages:

1. In the bipolar montage a sequential connection of channels along the anterior-posterior transverse rows is used. Thus, the potential difference between the two electrodes is measured.
2. In the monopolar or common reference montage each channels records between active scalp electrode and an 'indifferent' electrode usually on the chin, forehead or the ear, as long as it is far away from the actual recording site (Figure 20).
3. Joining all scalp electrodes to a common resistor of equal value, i.e. the average resistance, and measuring between this common reference and each channel, the average reference monitoring is used.

Commonly in anesthesia and in critical care one bipolar montage of each hemisphere is used, as this montage is able to:

– Measure the difference between both hemispheres.
– Evaluate the global ischemia of one hemisphere.
– Apply a limited number of electrodes as fast as possible.

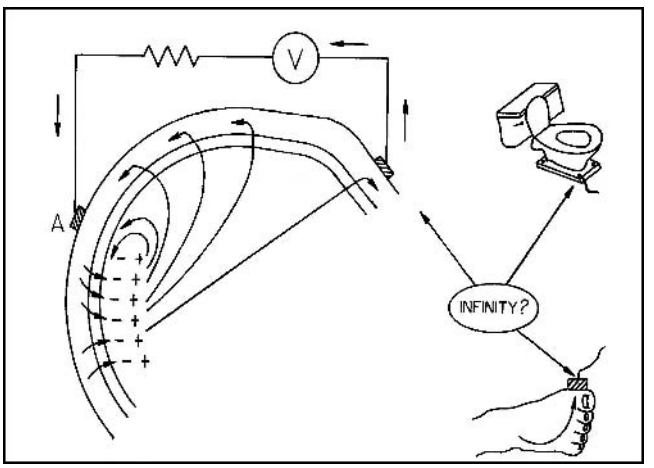


Fig. 20. Theory for localization of the indifferent electrode in order to measure a sufficient high voltage difference.

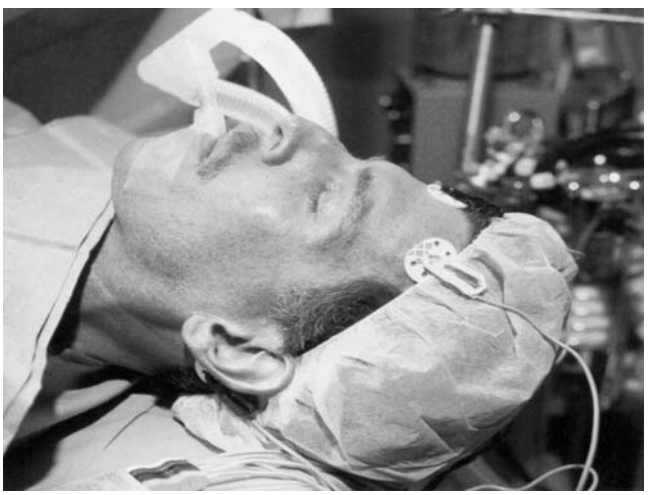


Fig. 21. Representative example of intraoperative bipolar recording with electrode positioning at location F_3 (forehead left side) – A_1 (behind the left ear lobe on the mastoid) using FpZ on the center of the forehead as the reference point.

Additionally, in cases of ischemia for instance due to carotid occlusion during carotid endarterectomy (CEA), widespread frontal and occipital EEG changes can be observed. This suggests that gross events can be monitored without complex montage [24]. Also, if electrodes are placed too close to each other, they do not necessarily pick up the potential changes directly beneath or between them [25]. For this reason a montage such as mastoid behind the era (A_1 and A_2 respectively as reference) and F_3 or F_4 as the active electrode in fronto-temporal recording, taking FpZ as the reference point, is sufficient to evaluate gross changes in cortical activity of both hemispheres, which are either due to the anesthetic or due to hypoxemia (Figure 21).

PROCESSING OF THE EEG – POWER SPECTRAL ANALYSIS

Strip chart is the conventional technique used in clinical neurology. A strip chart is written by an ink pen and moved by a paper drive. At a proper speed of 30 mm/s the machine produces 108 meters/h of recording paper! It is for this reason that computerized techniques have been developed to process and compress EEG data in cerebral monitoring. There are many methods for processing the EEG, but the most widely used method in intraoperative monitoring is frequency analysis. In this technique the EEG is seen as a simulation of simple sine waves with different frequencies. Frequency analysis mathematically decomposes this complex of sine waves with different frequencies into the various components using Fourier analysis. It was not until the rediscovery of the Fast Fourier algorithm by Cooley & Turkey in 1965 [12] that it became possible for computers to perform on-line power spectral analysis of the EEG. This mathematical technique is the fastest because of the fewer calculations in carrying out frequency analysis. Thus, a signal from 2–60 s, depending on computer capacity, is taken and frequency analysis is performed (Figure 22) using Fast Fourier Transform (FFT). The resultant analysis is recorded graphically; the power of the signal at each frequency is plotted vertically against the frequencies from 0–30 Hz. This produces a power spectrum of the original EEG signal. In the FFT mode the computer samples the EEG signal periodically over a certain period called epoch and converts that sample to a digital number of finite precision. The FFT method uses a fixed number of samples in that signal. At a 2 s epoch, for instance, 128 data points are sampled per second, thus yielding 256 data points per epoch.

Thereafter the distribution of energy or power at each interval of frequency is computed which results in the frequency spectrum of that sample. A procedure as outlined above produces a power spectrum of the original EEG signal. Plotting successive power spectra vertically so that changes over longer periods of time can be followed has further expanded the approach. The Compressed Spectral Array (CSA) format [26] combines high data compression and compact trending at the base activity and of the distribution of dominant frequencies and their evolution in time (Figure 23).

In the CSA mode sequentially calculated spectra are drawn with the aid of a plotter in a stack, each in front of the next. A hidden line suppression a1gorithm is usually implemented in the display to remove spectral information behind background feature to add a three-dimensional effect. Having the computer quantify certain aspects of the

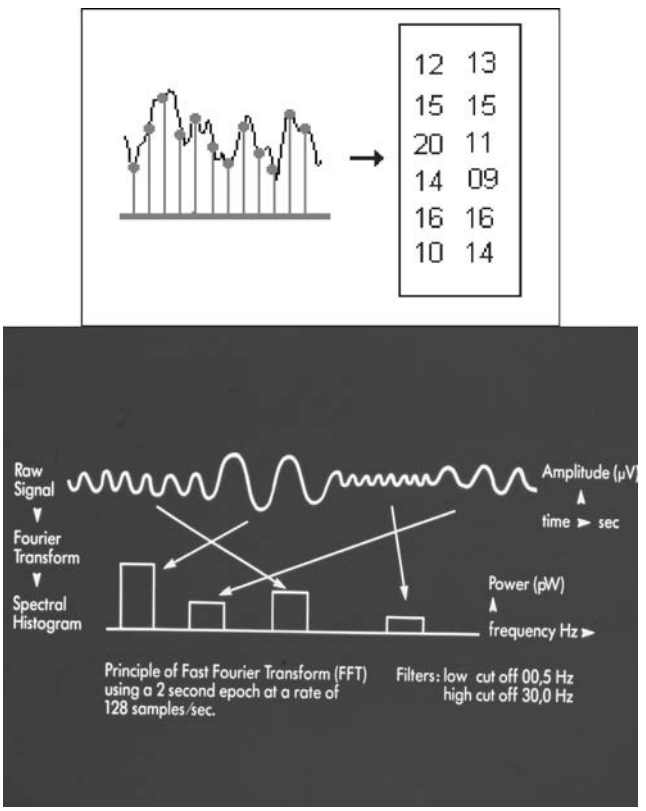


Fig. 22. Principle of Fast Fourier Transform (FFT) of the raw EEG. The original EEG wave is put into a digital format by sampling it repeatedly at very small intervals. The data of this epoch is then passed to the computer to perform FFT. As a result the amplitude of each frequency band is derived. In a final step the amplitudes are squared to give power, and plotted on a histogram depicting frequency on the x-axis and the amount of power on the y-axis.

computer spectra may make a further simplification of EEG interpretation:

– *Peak Power Frequency*: the frequency at which the highest power is found to occur in the current spectrum (Figure 28).
– *Median Power Frequency*: the frequency in the current spectrum at which half the power is above and half is below ([24]; Figure 24).
– *Spectral Edge Frequency*: the highest significant frequency present in the current EEG spectrum. This usually is the frequency, which represents 95% of all the power ([28]; Figure 25).
– the *ratio of power*, which computes the higher frequency bands alpha and beta to the lower bands delta this yielding a quick analysis of frequency changes in a given case (Figure 26)
– *Density Modulated Spectral Array* or DSA as originally proposed by Fleming is another way of evaluating power spectra with one glance [29]. In this technique the vertical axis is frequency and the horizontal axis is time. The relative power in the frequency bands is reflected in the density of dots. As time passes, a dot pattern develops with changing power content (Figure 27).

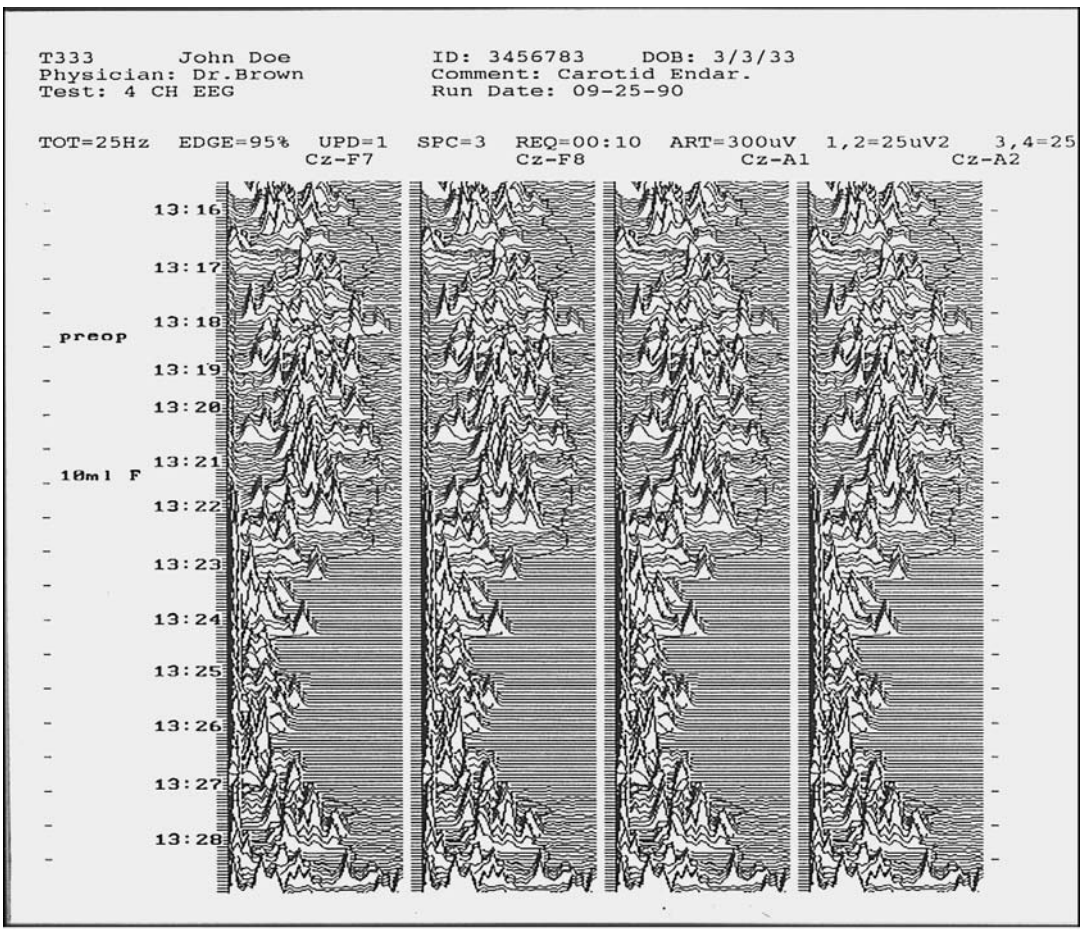
So far, all the univariate descriptors for intraoperative representation of cortical waves have been shown only to be accurate when the EEG behaves as an unimodal distribution of frequencies changing slowly with time. However, in the majority of cases these univariate descriptors of the EEG appeared inadequate to demonstrate changes of the EEG during anesthesia [17]. Further development in displaying the processed EEG in a three-dimensional manner with color delineation of the various frequency bands improved and aided EEG interpretation. This was realized in various other devices (i.e. Lifescan^{TM}, Neurotrec II^{TM}, etc.) or using other univariate descriptors such as the bispectral index (BIS), the spectral frequency index (SFx), the Entropy parameters, the Patient State Index (PSI) or the Narcotrend index (see chapter on "Systems currently available for processed EEG recording"). All these different parameters are able to differentiate the state of hypnosis during anesthesia, which usually is considered the level of anesthesia. They, however, in no way are able to directly reflect the level of analgesia. Only by means of an indirect way, when nociception results in a reflectory increase in vigilance this is mirrored in a reduction of the depth of anesthesia (Figure 28).

ARTIFACT REJECTION DURING PROCESSED EEG MEASUREMENT

An artifact is a sudden excess in voltage with respect to the average signals already occurred which, however, may not exceed the amplifier input dynamics. Artifacts of 30 Hz such as

– Power outlet noise, and most of all,
– Muscu1ar potentials from the tissue underlying the scalp (i.e. fronto-temporal montage),
– Loose electrodes, or
– Rapid ocular movements

are detected by an artifact rejection unit and identified as such. The electrosurgical or Bowie cauterizer noise is one of the most common generators of electrical noise. Bowie noise appears in the EEG as a complex mixture of very high-speed spikes and periods where the input amplifiers are saturated producing a flat line at one end of the scale. The spectrum may resemble that of motion artifacts, or it may appear in a diffuse high power distribution across the



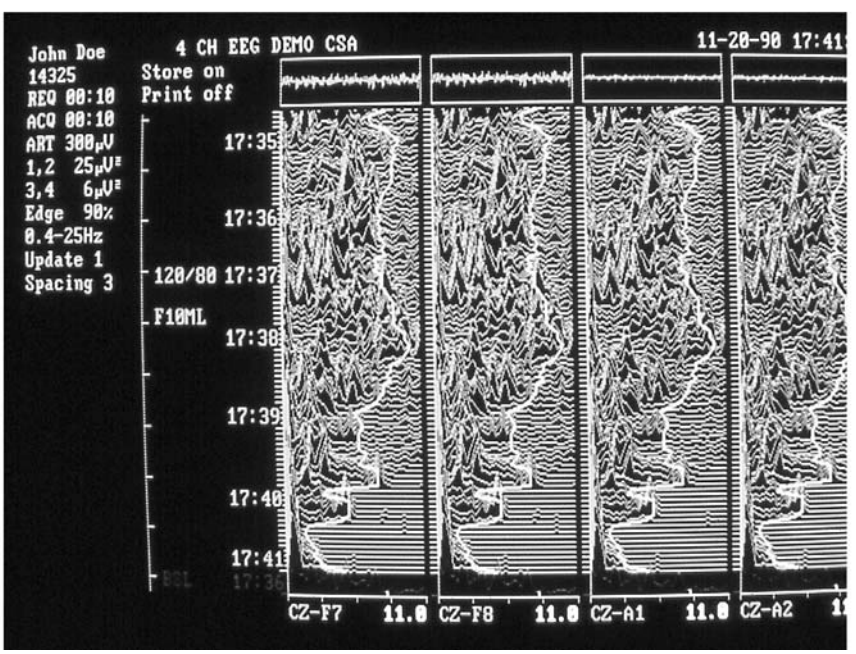


Fig. 23. Individual epochs of analysis are plotted closely above each other resulting in a "hill and valley" pattern. Such a picture is called Compressed Spectral Array (CSA).

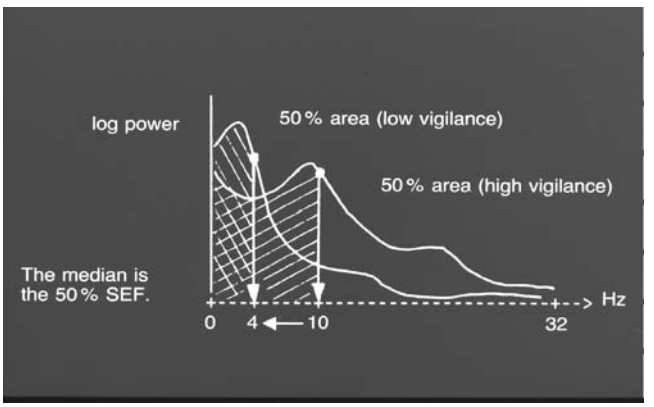


Fig. 24. Power spectra of the EEG and calculation of an univariate descriptor the median power frequency, which can be used to determine the state of vigilance in a patient after a sedative.

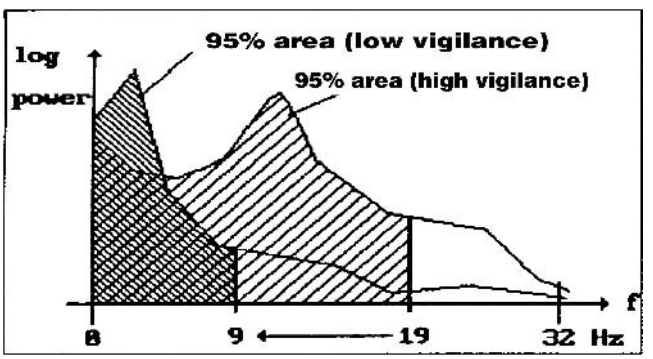


Fig. 25. Schematic presentation how Spectral Edge Frequency 95% (SEF 95) is calculated by using the area under the curve of the spectral histogram at different situations. High SEF 95 reflects high vigilance while low SEF depicts a depressed cerebral activity.

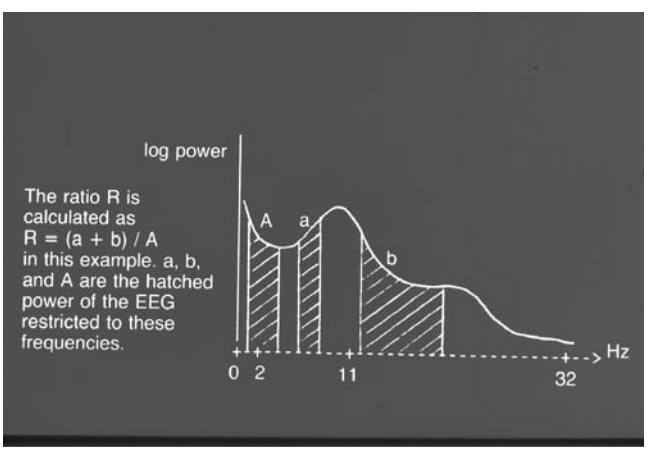


Fig. 26. The ratio of power calculating the power in the high frequency range against the lower frequency band delta, another possibility for univariate descriptor analysis.

entire spectrum. Interferences coincide with the application of the cutting or coagulation current. The following problems may be encountered during EEG recording in the 0R all of which interfere with the original EEG wave and its analysis with the aid of a computer:

1. Electrical interference

   (a) improperly applied electrodes,
   (b) electrocautery,
   (c) cell-saver machine, and
   (d) line interference from other electrical sources

2. Equipment failure:

   (a) major malfunction of the processor, and
   (b) malfunction of accessories.

SIGNAL CONDUCTION AND CONVERSION OF THE EEG

Most of the processed EEG machines used today run in a similar manner three phases in their operation cycle:

1. EEG conduction and conversion,
2. Data analysis, and
3. Formatting and display.

The EEG signal is collected from the scalp by disk, needle, or ECG electrodes applied in the same manner as for routine ECG examination. The low level signal which runs between 10–100 μV is amplified, filtered and checked for artifacts and sent to an analog-to-digital converter. The amplifiers are low-noise, high-gain differential amplifiers with a high impedance front end. After amplification the signal then is filtered by a third low-pass filter with a cutoff (2 db down) at 30 Hz and by a fast-order highfilter with a cutoff at 0.5 Hz (high pass filter) giving a passband of 0.5–30 Hz. The filtering serves to reduce the noise picked up along with the EEG by the sensitive amplifiers. Two EEG channels then usually are multiplexed and sent to the analog-to-digital converter on a first procedure board.

The incoming signal is sampled at 256 Hz giving a sampling rate of 128 Hz per channel. Samples are converted to bit words, separated into two channels and stored by the microprocessor. Artifact detection is performed by means of a three-part algorithm, which checks for:

1. EEG signals too high for the amplifiers.
2. A zero derivative signal, and
3. 60 or 50 Hz noise.

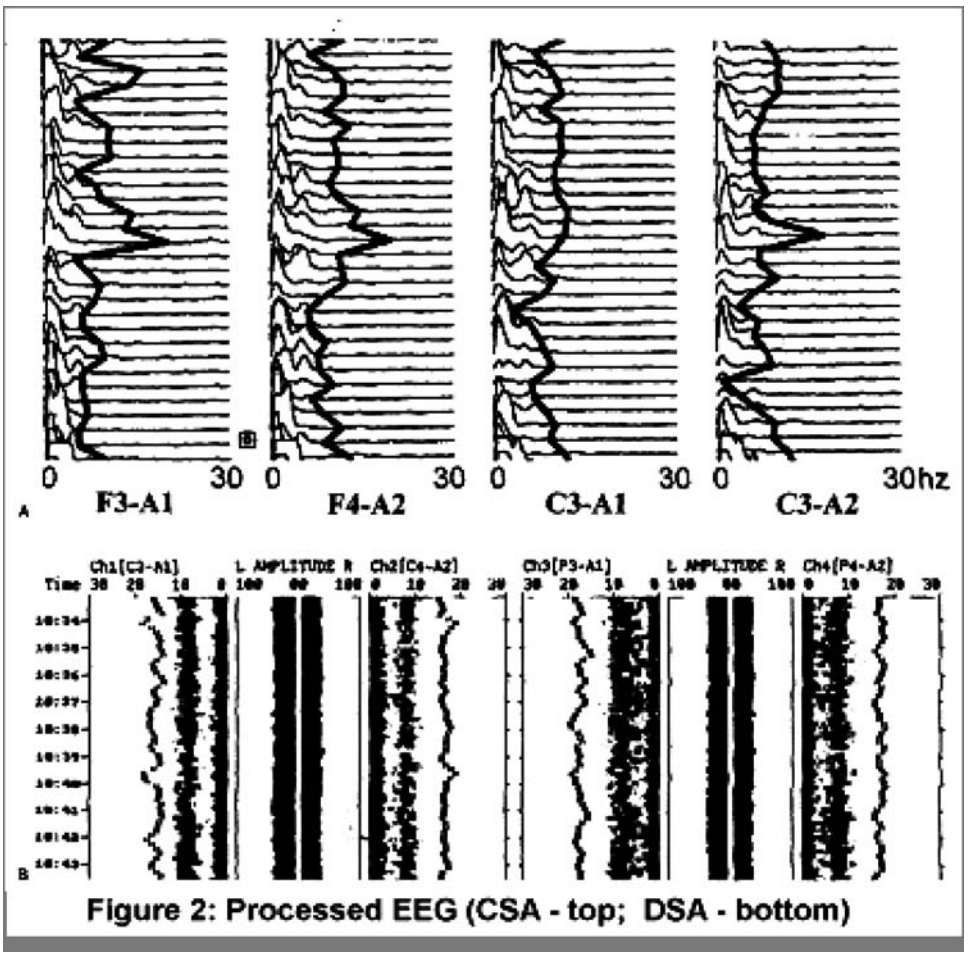


Fig. 27. Examples of the processed native EEG depicting the Compressed Spectral Array (CSA) and the Density Modulated Spectral Array (DAS) for quick overview of EEG activity, for instance, in the OR.

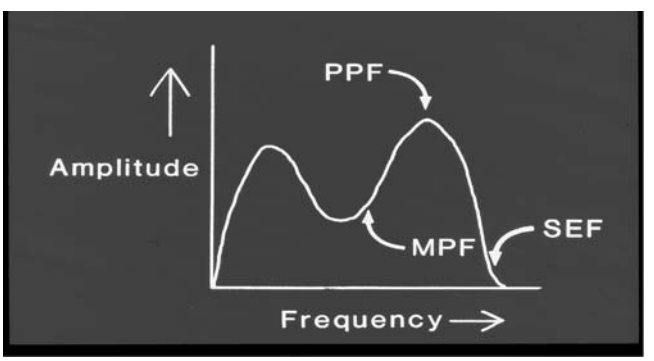


Fig. 28. Summary of the various attempts to simplify analysis of EEG power spectra. Median Power Frequency (MPF) is the frequency, which bisects the power curve. Peak Power Frequency (PPF) is the frequency, which comprises the largest single component of the power spectrum. Spectral Edge Frequency (SEF) is the highest frequency component in the EEG.

The presence of artifact is flagged in several ways on the screen in each display mode for each channel. The raw EEG signal is available for display on the screen whenever a specially designated key on the keyboard is pressed. Most devices analyze the raw EEG using the Fast Fourier Transform (Figure 29), while only one device uses the Aperiodic Analysis. The resulting spectra along with the raw data are sent to the display processor. In the Fast Fourier Transform (FFT) mode, the spectral results of epochs 2 second each (=256 data points) are used. Contrary to the FFT episodes, Aperiodic Analysis of the EEG [25] yields an estimate, where amplitude and frequency are presented on a wave-by-wave basis (Figure 30). By the latter method, a wave is defined as a fluctuation in voltage that occurs between two local minima in voltage. Thus, the algorithm scans through time for decreasing voltages. When an increase in voltage is identified relative to the previous point,

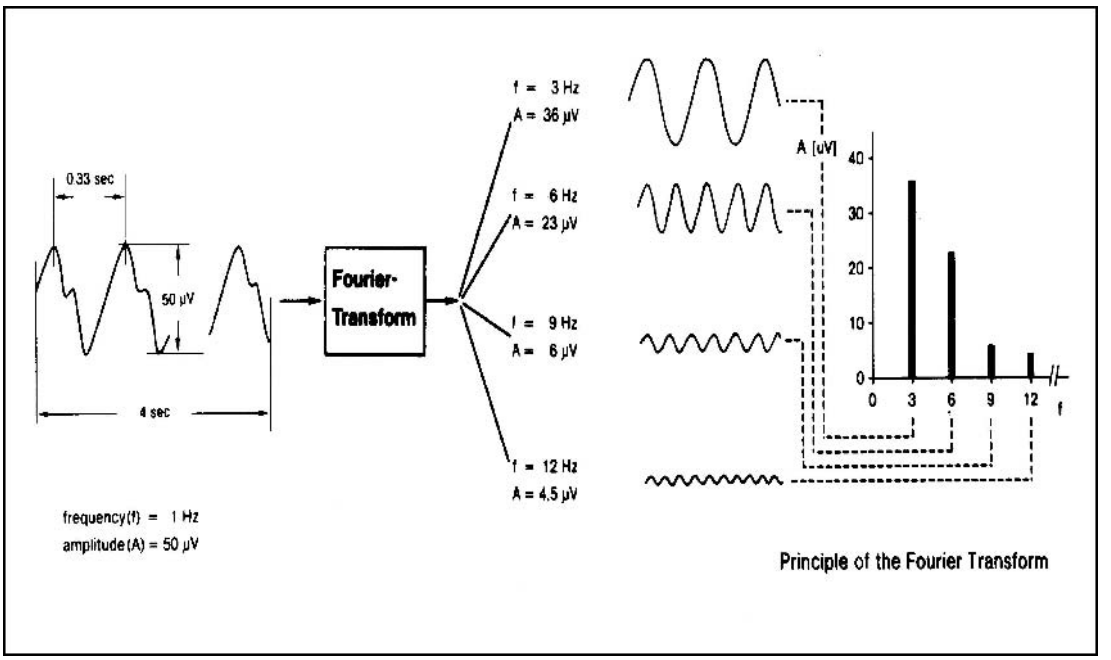


Fig. 29. The principle of Fast Fourier Transform (FFT) of the EEG signal resulting in power spectra.

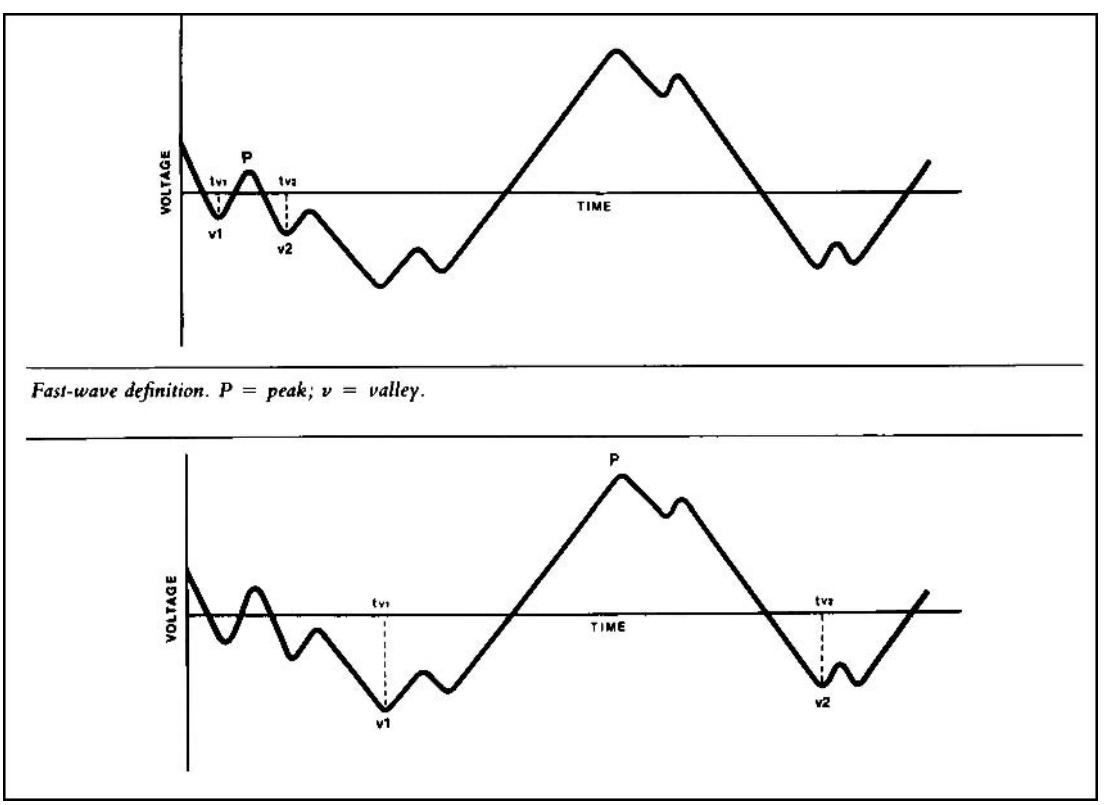


Fig. 30. Principle of algorithm using aperiodic analysis of the EEG. The amplitude of the waves is defined as the average difference in voltage between P and V_1 and the difference in voltage between P and V_2. The power as it is visualized in a vector $(\mu V) = (VP - V_{V1}) + (Vp - V_{V2})/2$. Frequency of the wave is defined as the inverse of difference in time between minimal V_1 and V_2 Thus frequency (Hz) $1/(t_{V2} - t_{V1})$. Abbreviations: P = peak; V = valley.

then the previous voltage is noted to present a minimum valley V_1 while scanning along as the voltage increases. Relative to the previous time point, any increase in voltage thereafter, the local maximum peak P of voltage is identified (Figure 30). To detect slow delta or theta waves in the presence of high frequency waves, a slow wave method is used similar to the technique as described above [30], except that it scans for the largest valleys and peaks between zero voltage crossing (Figure 30). In addition, each channel samples the signal 960 times per second compared to the usual 128 used by most of the other algorithms resulting in a higher resolution.

Aperiodic Analysis seems to result in better representation of EEG waves of short duration. Thus, fast waves with small voltages, which, however, may be important in the clinical setting, are preferred. By comparison, FFT obtains a spectral representation of the EEG, which, due to the stochastic nature of the EEG waves, is not logical. As EEG waves do not seem to present a mixture of regular sinusoidal-waves, but more like random non-periodic fluctuations, other forms of computation of power in the EEG are likely to be more rational, reflecting the real nature of the signal. Additionally, the finite period of epochs during which data is collected with the FFT reflects spectral representation, missing those intervals at which changes may have happened. A technique with an averaging, smoothing mode, alters the accuracy and resolution of the resultant frequency spectrum [31]. Independent of the nature of EEG analysis and the type of algorithm being used, all EEG data can be formatted and displayed in one of three different formats when using the FFT or in one of the two different formats when using the Aperiodic Analysis:

1. The raw EEG signal.
2. A bar graph of each channel power spectrum (FFT algorithm), or as an amplitude and frequency information as used in the two-dimensional screen with a color vector and a three-dimensional time axis into the depth of the screen as time progresses (Figure 31).
3. Compressed Spectral Array (CSA) with power spectral lines taken at successive time intervals on the screen to produce a quasi three-dimensional trend (Figure 31).

Independent of the type of EEG algorithm being used, the displays on the screen offer a number of options:

1. Display of a single channel or both channels of the native EEG waves on screen.
2. Updating the time from a two-second analysis to several minutes.
3. Storage of analyzed data up to several hours.
4. Display of Spectral Edge Frequency (SEF), the location in the power chart where the processor draws a line reflecting a point (Hz) in the spectral content which incorporates a certain amount (usually 95%) of total power.
5. Change in the gain setting for the power values in the spectral histograms.
6. Menu-driven check of impedance of all electrodes attached to the scalp.
7. Display of power bands and/or power vectors in the various frequency bands.
8. Computation of the absolute power values (nanoWatt, microVolt^{2}or μV^2), which can be printed on paper by a built in plotter.
9. Extension of cerebral monitoring to the Evoked Potential Mode in order to evaluate the function of somatosensory pathways in deeper, subcortical brain structures.
10. Use of the EEG analysis device as a system to process raw EEG signals from tape or a regular EEG machine.

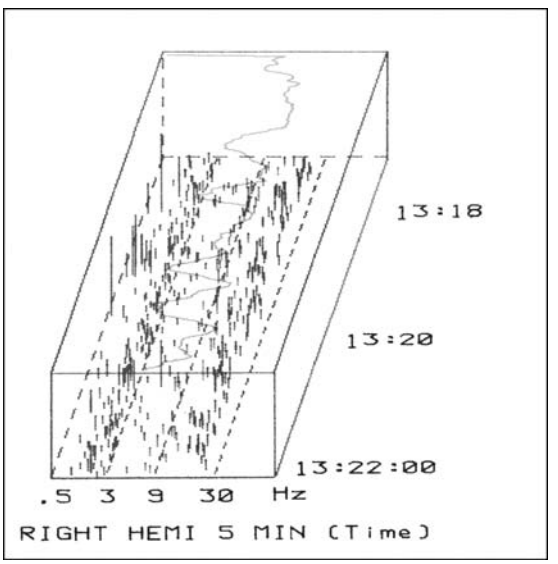


Fig. 31. Representative example of computerized EEG power spectra taken postoperatively from a patient after enflurane anesthesia and induction with midazolam. Aperiodic analysis denotes fluctuation of vigilance, which is best seen by the spectral edge as it changes along with time, suggesting an overhang of benzodiazepine action.

Basically, computerized EEG recording consists of five subunits (Figure 32):

1. The preamplifier, which is connected to the processor via lines and enhance the brain waves taken from electrodes on the patient.
2. The microprocessor for data conversion, analysis, and formatting.
3. The display board or screen containing a screen for black and white or color processing of results.

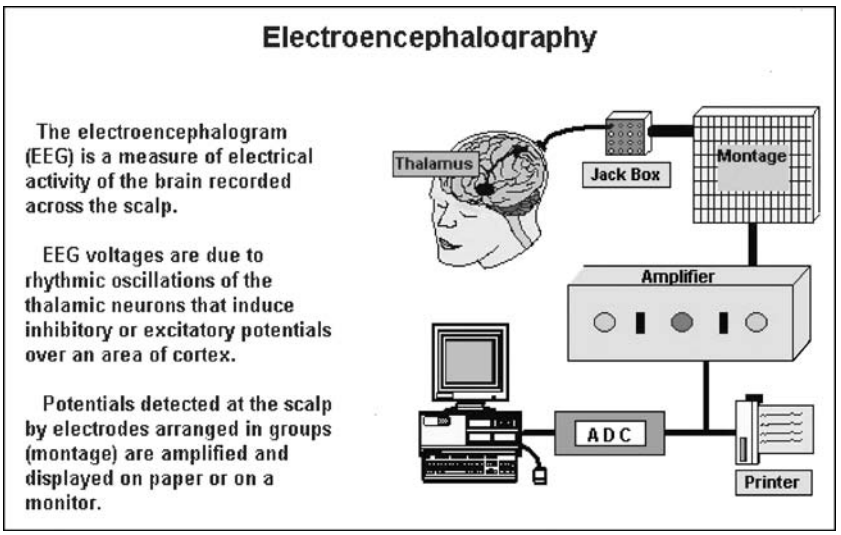


Fig. 32. The basic components in processed EEG monitoring from the CNS to the computer display.

4. The printer or plotter for permanent plotting of relevant data.
5. The keyboard with numbers and/or different color-coded digits to operate the monitor and select the montage.

SET-UP FOR MONITORING THE EEG; THE ELECTRODE MONTAGE

This chapter describes the electrode positions on the scalp, and the cable connectors when wanting to use an EEG monitor in the operation room and/or the intensive care unit. Before one sets about monitoring the brain, it is important to note that the 12 to 16 lead EEG usually used in neurology and psychiatry, is not mandatory during anesthesia and critical care. Since localized changes are of no significance to the anesthesiologist and/or the intensive care therapist, only 2 leads, one of the right and one of the left hemisphere, are necessary to obtain a picture about global changes that occur in the brain. Thus, the effect of anesthetics in the brain and of ischemic events can be recorded with sufficient ease for routine use. The computer-run monitors have to fulfill basic requirements in order to become a useful tool for the clinician. In order to become a useful unit it has to comply with certain clinical requirements:

1. Is compact to fit into the operation room and the intensive care ward, designated to share the sparse room with other electronic equipment,
2. Is mobile on rollers so that it can be easily wheeled from one place to the other,
3. Is simple in operation, preferably using touch keys,
4. Contain a view screen with sufficient resolution in contrast for changes to be viewed from a distance,
5. Contain an input/output terminal for system expansion (preferably a RS-232 serial or a USB port),
6. Contain memory capabilities for at least 12–24 h recording of patients in the intensive care,
7. Allows storage of snapshots of EEG events for later retrieval via the built in plotter or printer,
8. Monitor the impedance continuously in order to affirm sufficient electrode contact,
9. Contain on-screen a self-explanatory user guide after switch on,
10. Store, for later retrieval and comparison, a number of typical preprocessed events that are stored in the data bank permanently, to aid the clinician in decision making, and
11. Have the option of permanent data storage on floppy disk or CD.

In order to facilitate and speed up electrode positioning, three frontal electrodes at positions F_3 (+) and F_4 (+) with the reference pole at the forehead are used, while the negative pole (−) is applied on the mastoid of the respective side (Figure 33). Each electrode position has a standard abbreviation based upon the brain area it represents. The letter designates the underlying brain region to which the electrode position corresponds. The odd numbers designate the left side of the head; an even number designates the right side while "Z" designated the mid-line.

Care should be taken in the preparation of the skin underlying the electrodes:

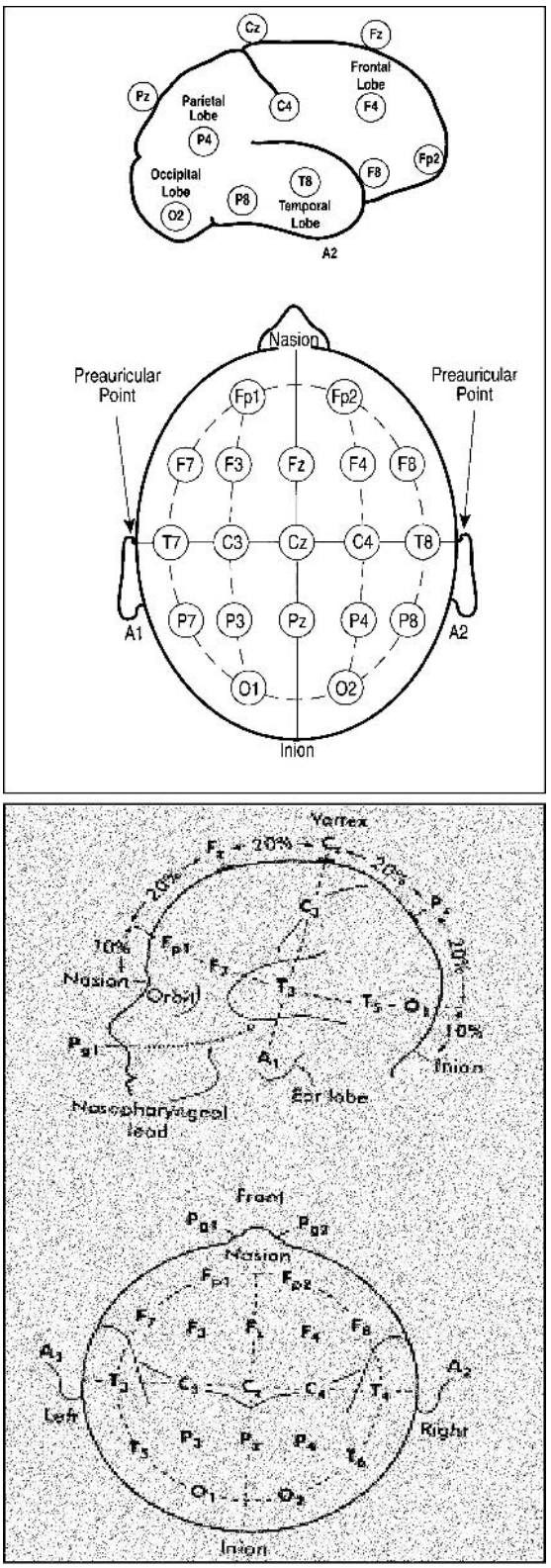


Fig. 33. Nomenclature for electrode montage on the scalp for recording of EEG activity.

(a) Select hair-free skin site,
(b) Clean site of application with a mild abrasive cream (e.g. Omniprep^{TM}) using a cotton tip applicator in circular motion to abrade the skin,
(c) Use alcohol to wipe off the abrasive cream and to further clean the site application,
(d) Next use a dry gauze and rub briskly to dry the area,
(e) Ensure that the skin is completely dry before applying the self-adhesive EEG electrodes,
(f) Remove the release band of the electrode taking care to minimize finger contact with adhesive areas,
(g) Ensure that the center pad is sufficiently moistened with electrode gel, and
(h) Apply the EEG electrode utilizing finger pressure around the adhesive area a circular motion (Figure 34),
(i) Snap the shielded leads to the electrodes,
(j) Connect the colored leads with the similarly color-coded sites on preamplifier,
(k) Gather the wires to the preamplifier together and place tape around them to secure together. This will help to prevent accidental dislodging as well as help to minimize movement artifacts and pick up of 60–50 Hz interference
(l) Check impedance. If unacceptable impedance occurs, identify the electrode, which might be responsible and replace it by repeating steps (a) to (k); if impedance is still high, one lead must be faulty and needs to be replaced.
(m) Clamp the preamplifier to the bed linen near the patient,

Fig. 34. Procedure as how to accurately identify the electrode position and mark its location on the skin with a grease pencil, using the 10/20 system and a centimeter band.

(n) Check for crossing of shielded leads with other electrode wire (e.g. ECG) to avoid interference, and
(o) Use the touch key for activation of the raw EEG signal display, making sure that both channels show a good reading without the EEG waves wandering over the screen.

Only now processing of the original EEG can start. For optimal evaluation of cortical activity and to guarantee an artifact-free recording over a long period, every time the EEG is monitored and the raw signal is processed for data comprehension and reduction, steps (a) to (n) must be followed meticulously. In addition it is important to point out that the EEG "only" reflects potential changes between the two selected electrode sites of the upper 2 cm of cortical layers. The EEG *does not* reflect functional deficits or changes in the deeper, subcortical structures. For the evaluation of deeper brain structures see the chapter on Evoked Potential Monitoring.

Always remember:

Dry skin = positive skin contact = low impedance = reliable signal for monitoring!

In cases where the patient is perspiring profusely, self-adhesive electrodes tend to lift off, resulting in a deterioration of the raw EEG signal and a wandering of the base line, which in a number of cases is detected by the algorithm as slow EEG activity and not as an artifact (!). In such circumstances use of silver/silver chloride cup-electrodes are recommended, which are fixed to the skin by means of a special glue (collodion). For ease and speed of application, a reciprotor pump is advocated which quickly dries the glue, which previously has been applied around the flanges of the cup electrode (Figure 35).

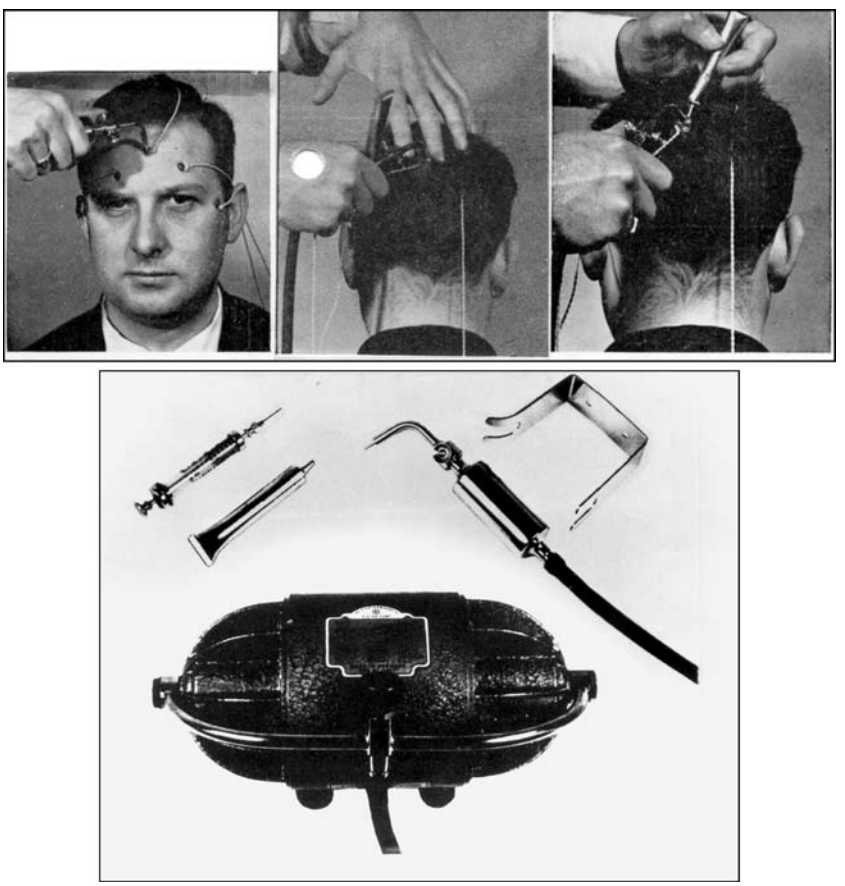


Fig. 35. The reciprotor pump blowing dry air on the cup electrode, which is glued to the scalp by means of collodion.

ANESTHESIA AND THE EEG

Rationale for the use of the EEG in anesthesia

The use of the EEG in anesthesia originally evolved from the hope that it would be possible to define the anesthetic depth by reference to the EEG pattern, irrespective of the agent being used. Of greater importance, aside from the ease of interpreting the EEG signals with the above-mentioned menu-driven computations is, however, the speed of response to ischemic events, which can be visualized on the EEG screen. Such events can occur very rapidly during surgery, at a state where anesthesia covers the events to such a degree that the sequelae will only become noticable when the patient regains his consciousness. The common EEG-pattern sequences as they occur with increasing depth of anesthesia are as follows:

1. In the resting state the marked variation that exists in the EEG among awake, normal subjects disappears,
2. The EEG tends to appear as a common pattern in all anesthetized patients.
3. The changes under anesthesia are generalized, so that electrode placement on the scalp is not critical and in general a pair of widely spaced electrodes will be sufficient to reflect a representative record. All these facts greatly simplify EEG comparison under anesthesia,
4. Initially, anesthetic agents increase electric output of the brain and, after a peak is reached, there is progressive reduction with increasing anesthetic depth (early burst suppression), until finally, the EEG becomes totally flat, devoid of any activity (late burst suppression) to total EEG suppression (Figure 36).

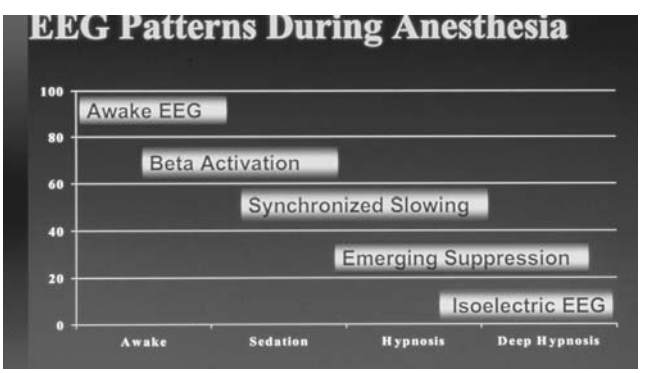


Fig. 36. EEG pattern with increasing depth of anesthesia. The graph shows the change in integrated voltage output related to pattern changes with increasing depth of anesthesia. With certain ether agents such as enflurane, a stage of seizure activity may follow the suppression. Modified from [32].

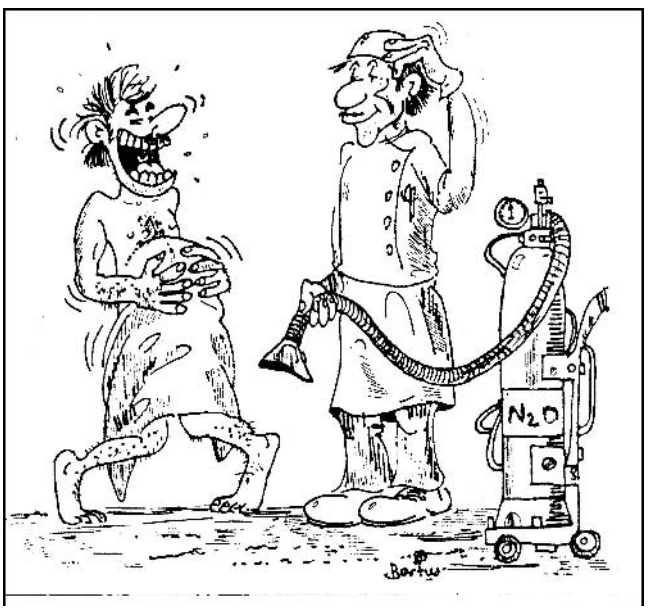


Fig. 37. What do you expect from an anesthetic like nitrous oxide.

However, some volatile anesthetics, especially those of the ether type, develop a different pattern beyond suppression, which is characterized by generalized seizure activity with increasing concentrations. In modern anesthetic techniques using balanced anesthesia with different compounds, interpretation of the EEG in regard to the anesthetic depth tends to become difficult. This is primarily due to the combination of drugs affecting different levels of the brain. Thus, determination of absolute levels of anesthesia is difficult to assess with the use of multiple agents on board; however, shifts of the depth of anesthesia can almost always be seen (Figure 36).

Inhalational agents and their effect on the EEG

Nitrous oxide (N_2O)

Up to 30% of nitrous oxide in the inspired air results in minimal changes in the EEG in spite of the marked psychological disturbances that can be observed (Figure 37). At 50% unconsciousness develops with increasing disappearance of alpha rhythm with interposed short episodes of fast beta activity. This is followed by the appearance of slow theta (4–7 Hz) activity, while at 80% N_2O fast activity disappears totally and only theta remains in the EEG picture [33–35].

Halothane

Subanesthetic levels of halothane produce a fast 12–18 Hz pattern in the EEG, which continues, as consciousness is

lost. At 1 MAC (=0.84 Vo1%) the dominant activity falls between 11–16 Hz. As anesthesia deepens there is a near linear decrease of EEG rhythm by about 1–1.5 Hz with each 0.5 MAC (=0.42 Vo1%) halothane concentration. Above 2 MAC, EEG power in the delta band arises from background activity until finally at 4 MAC, almost all activity is centered on the 0.5 Hz level [29]. If nitrous oxide is given together with halothane, the degree of slowing in the EEG is augmented. Thus, unconsciousness occurs when the EEG activity is centered around 12–15 Hz (=alpha), while surgical stimulation is tolerated at peak power frequencies between 6–8 Hz (=theta) [13, 36].

Enflurane

The electroencephalographic changes seen with enflurane are in many ways identical to the changes seen with the other inhaled anesthetics: an increase in the concentration decreases frequency and increases voltage [32]. At concentrations of 1 MAC (=1.7 Vol%) the EEG dominance is of slow waves with high amplitudes in the 4–8 Hz range. The waves further slow as anesthesia deepens while early burst suppression periods occur at 1.5 MAC. This is specifically the case when low pCO_2 levels are present; the EEG picture may be interrupted by the appearance of occasiona1 high voltage spike waves (Figure 38). In deep enflurane anesthesia (2–3 MAC), especially when inducing high concentration of the anesthetic such as during mask induction in an infant, epileptic-like single bursts or groups of bursts become apparent (Figure 38). These are followed by 5–15 s of isoelectricity, associated with or without abnormal muscular movements The latter are manifested by twitching of individual muscle groups [32, 37, 38].

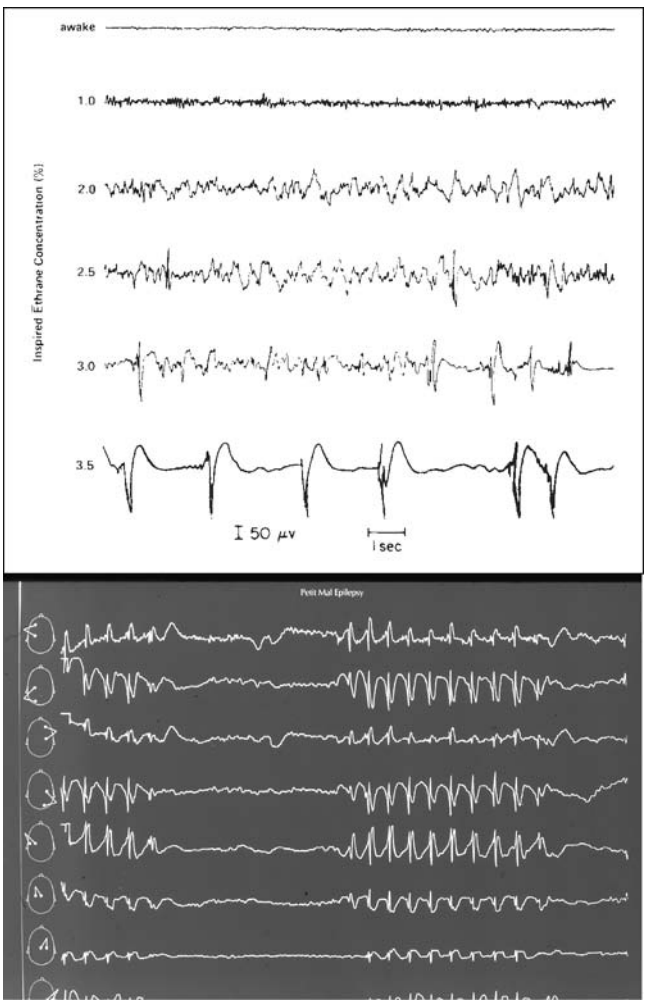


Fig. 38. Increase in inspired enflurane concentration results in a decrease of frequency and increase of amplitude of the EEG. At 3–3.5 Vol% burst suppression occurs. Also, at 3.5 Vol% spike and dome activity may be observed (adapted from [37]).

Isoflurane

Pharmacologically, this volatile anesthetic agent is a structural isomer of enflurane, which induces a similar EEG pattern as enflurane (Figure 39). However, this halogenated methyl-ether does not elicit the burst-like pattern in the EEG at 2–3 MAC (=2.4–3.6 Vol%). With deep isoflurane anesthesia there is dominant power in the delta range, which may be followed by electrical silence of several seconds [38].

The capacity of isoflurane to produce an isoelectric electroencephalogram and the absence of seizure activity sets this volatile compound apart from the other inhaled anesthetics. Although ether also can produce an isoelectric pattern, the concentration required (in MAC multiples) is significantly greater. In addition, ether agents can produce a convulsive EEG pattern, which may appear at concentrations only slightly higher to produce an isoelectric pattern (Table 1 adapted from [32]). The effect of loss of EEG activity during anesthesia can be considered as a sign of deep anesthesia.

Table 1. MAC multiples required to produce an isoelectric and/or a seizure pattern in the EEG of man with different anesthetics

Anesthetic agent	Isoelectricity	Seizure activity
Isoflurane	2.0	0
Ether	3.5	4.5
Halothane	3.5	0
Enflurane	0	2.0–3.0

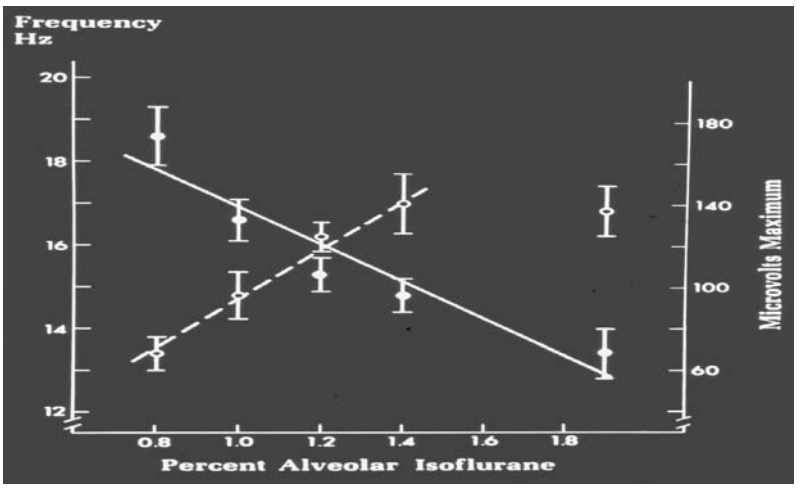


Fig. 39. Amplitude (open circle) and frequency (closed circle) changes in the EEG with increasing concentrations of Isoflurane. Adapted from [39].

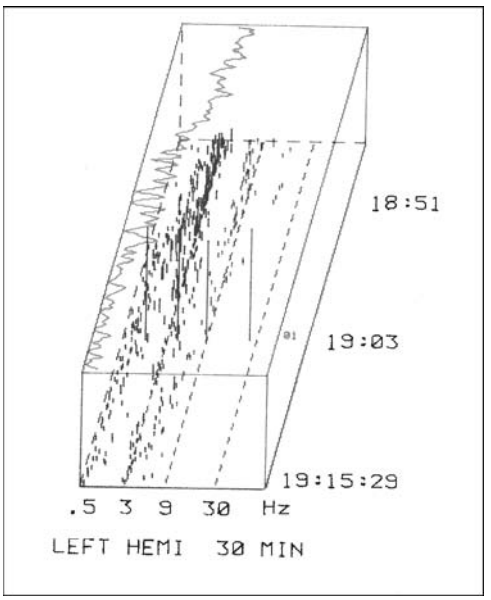


Fig. 40. Example of intraoperative EEG monitoring where a deep anesthetic plane was detected and corrected (EEG power spectra derived with the Lifescan™ cerebral monitor). X-axis = frequency band (Hz) Y-axis = amplitude height (gain 100 μV) z-axis = evolution in time (minutes) enflurane 0 Vol%; N_2O/O_2 = 2/1; Spectral Edge 0.5 Hz.

In a representative example of a white female 68 years of age undergoing gall bladder removal, enflurane-N_2O/O_2-anesthesia with 2 Vol% produced a dominance of delta waves in the EEG power spectrum (Figure 40). This is clearly marked by the spectral edge frequency (SEF), which centers around 3 Hz. At 18:51 h without any change in blood pressure and/or heart rate, EEG activity suddenly dropped. This is depicted in the power spectrum with a drop in the SEF to 0.5 Hz and a marked depression of amplitude in the delta range. Subsequently, enflurane concentration was reduced to 0 Vol%, which resulted in the reappearance of power in all frequency bands. At the end of the surgery the patient recovered uneventfully.

Without the use of the EEG monitor this deep anesthetic plane would not have been discovered and eventually would have led to cardiovascular depression and/or prolonged awakening from anesthesia. The difference of structurally similar anesthetics, enflurane and isoflurane, on EEG activity can also be seen in patients undergoing CABG (coronary artery bypass grafting) with hypothermia. During the cooling period there is a temperature-related depression of the EEG, in spite of constant blood anesthetic concentration.

During rewarming and continuous enflurane administration, the EEG power in the theta band (4–8 Hz) is characterized by a marked increase at a point where body temperature reaches 30 °C. This is in contrast to isoflurane anesthesia. Rewarming of body temperature is characterized by a gradual increase of power in the theta band. The former may be interpreted as "benign convulsive activity" with a mean power difference of 345% in the isoflurane as compared to the enflurane group (Figure 41).

The difference in EEG power spectra during rewarming when administering either enflurane or isoflurane is summarized in the following figure demonstrating the results derived in 10 patients undergoing AC-bypass operation and where anesthetic blood levels were kept constant throughout the rewarming period (Figure 42).

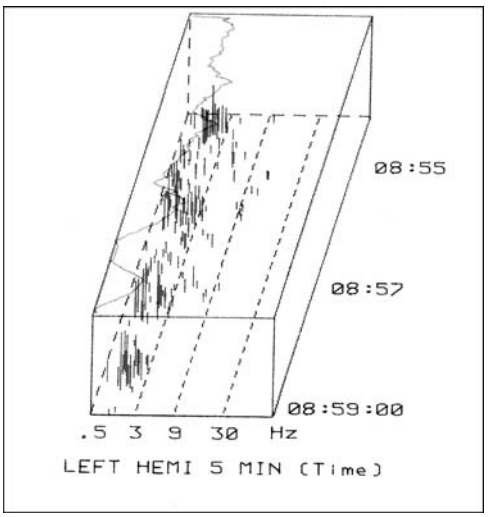


Fig. 41. Representative example of a patient undergoing AC bypass operation with hypothermia. With the start of cooling there is a remarkable decline in EEG activity, which eventually will result in intermittent bursts of depression as demonstrated in the changes in spectral edge frequency over time.

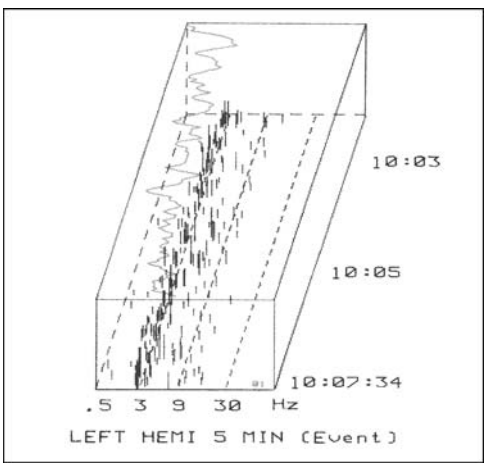


Fig. 42. Effect of rewarming on the various EEG power frequencies of the EEG in a patient undergoing AC by-pass operation with hypothermia. From short periods of burst suppression there is a gradual appearance in the higher frequency range, resulting in a higher spectral edge (red line).

The increase of power in the beta band during rewarming is far greater than the increase of power in the alpha and theta domain. The cause of this difference is probably the decrease of carbon dioxide during cooling. Thus, enflurane tends to induce an increase of EEG activity, which is closely correlated with an increase in cerebral oxygen uptake as demonstrated elsewhere [40]. As with the other volatile agents, addition of N_2O results in an increase of the anesthetic effect (Figure 43).

Carbon dioxide (CO_2)

The effects of CO_2 on the EEG vary according to the $paCO_2$ level. While 30% inhaled CO_2 result in an intermittent epileptiform discharge, higher concentrations of 50% produce electroencephalographic depression in the animal. Hypercarbia at a steady halothane level and contrary during enflurane anesthesia results in slowing of the EEG [41]. The addition of CO_2 to the anesthetic mixture is often advocated to prevent episodes of spike-like patterns [42]. These changes brought about in the EEG by enflurane differ from other agents. Since hypercarbia deepens anesthesia, it may also function as a form to prevent a spike-like pattern in the EEG. If burst suppression is present, the suppression pattern is lengthened and the burst shortened as CO_2 is introduced. However, during enflurane anesthesia, hypocarbia lengthens bursts and shortens the suppressions. Thus hypocarbia can be considered as an adjunct to enflurane, which potentiates the initial central effects of the inhalation agent while the epileptiform components are reduced [37, 43].

Desflurane, Sevoflurane

Similar as in isoflurane, increasing concentrations of both agents result in a concentration related increase of power in the slow delta-band and a concomitant decrease of power in the fast beta-domain (Table 2). Also, during deep anesthetic levels early burst of suppression may become apparent.

Aside from their effect on the electroencephalogram there is a close correlation between decrease in beta-power and heart rate ($r^2 = 0.988$) and systolic blood pressure ($r^2 = 0.952$) when using both agents (Figure 44).

Table 2. Grand mean changes in normative power (%) in the various power spectra of the EEG in patients receiving either desflurane or sevoflurane in nitrous-oxide/oxygen

	Desflurane		Sevoflurane	
Power range	1	2 MAC	1	2 MAC
Delta (0.5–3 Hz)	65.0*	72.0**	45.0	71.2**
Theta (3–8 Hz)	13.0	13.2	16.6	19.9
Alpha (8–13 Hz)	24.9	10.1*	12.0	3.9**
Beta (13–30 Hz)	13.0	5.0**	12.3	1.4**

Note. Significant differences of MAC 1.0 and MAC 2.0 to control (*$p < 0.05$; **$p < 0.001$; adapted from [44]).

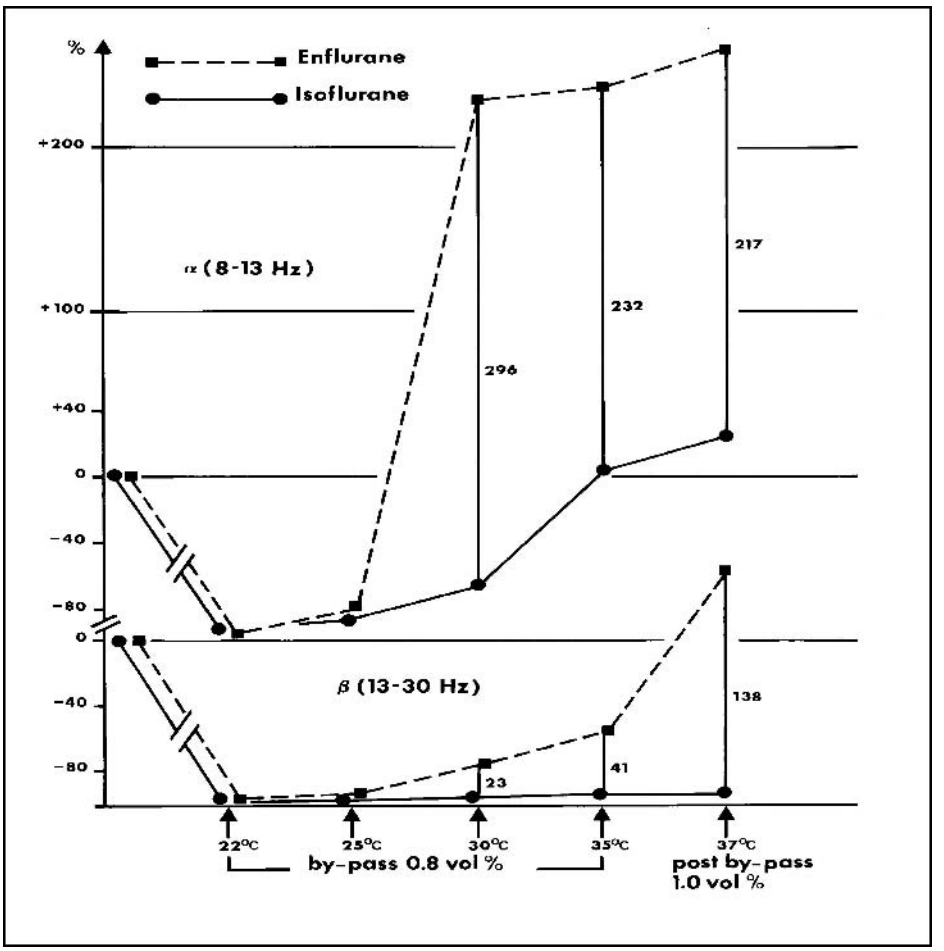


Fig. 43. Summary of power spectra in the fast alpha- and beta-domain during rewarming in patients with CABG. Note the increase of power in the beta- and alpha-band in patients ($n = 10$) receiving enflurane- compared to patients ($n = 10$) being anesthetized with isoflurane-oxygen anesthesia.

Intravenous agents and their effect on the EEG

Barbiturates

The injection of a short acting barbiturate initially produces fast 15–30 Hz waves. Thereafter, 5–12 Hz waves superimpose themselves on the fast waves often in spindle-shaped bursts. Next, high-amplitude 1–3 Hz waves develop indicating a depth of anesthesia at which skin incision is tolerated. If the barbiturate is given rapidly in a bolus, the earlier stages may be by-passed and delta waves will first appear. Increasing the dose of the barbiturate results in burst suppression in which the suppression period progressively is lengthened as the dosage is increased until electrical silence occurs. Within the first seconds following injection of a barbiturate slow delta to theta waves develop while, simultaneously, often heart rate increases. The latter is considered to be related to a desinhibition of brain stern structures involved in cardiovascular control. It is suggested that barbiturates reversibly block the synchronizing influence of lower brain stem structures, which results in a preliminary EEG arousal with fast activity and an increase in heart rate. As the barbiturate reaches midbrain structures and the rostral parts of the encephalon, a synchronized pattern results dominated by spindles [45].

Etomidate

Use of the induction dose of 0.3 mg/kg results in an overlapping of four EEG stages. First there is an increase in alpha amplitude followed by a mixed theta activity. Second there is mixed theta to delta activity while in the third stage consistent delta waves are apparent. In the fourth stage burst suppression appears [46]. Myoclonic and tonic movements, resembling those of seizures in some patients, are not associated with seizure activity in the EEG [46].

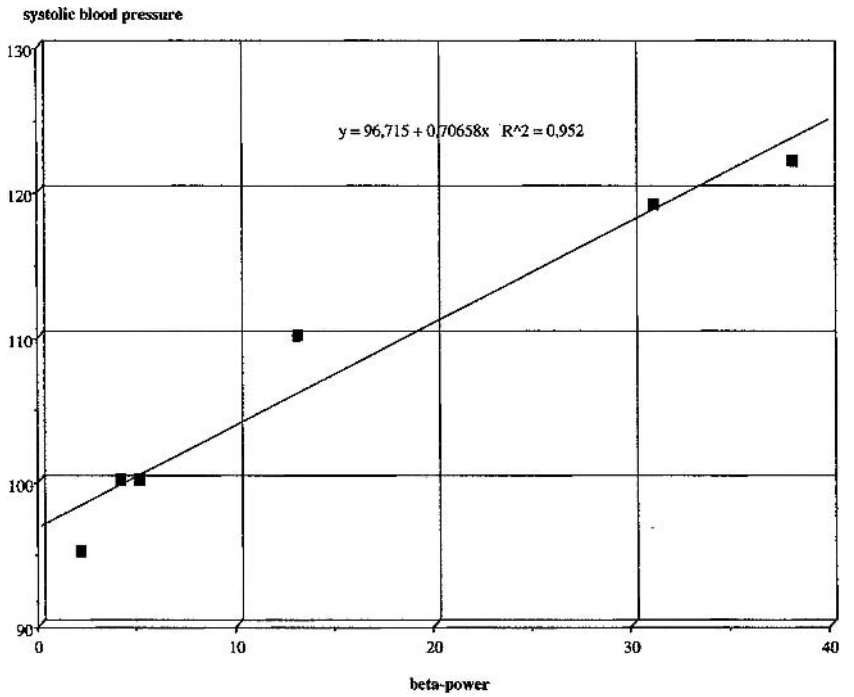


Fig. 44. Linear correlation between systolic blood pressure and power in the beta-band of the EEG using multiple MACs of either desflurane or sevoflurane in gynecological patients. Adapted from [44].

Opioids

While opioids, as they are used for premedication, have little effect on the EEG. High doses as they are used in techniques for cardiovascular surgery, result in a fall in frequency and in an increase in amplitude. The resultant dominant delta activity is demonstrated in a patient scheduled for elective cardiovascular surgery, who received 0.3/70 kg mg of the potent opioid fentanyl for the induction of anesthesia (Figure 45).

Such effects are not only associated with fentanyl, they are also seen after the short-acting narcotic alfentanil, high doses of morphine (1–10 mg/kg), and after moderate doses of sufentanil (15–30 μg/kg) [47–50]. With increasing concentrations of the opioid at the receptor site in the CNS, delta waves become dominant. This effect of CNS-changes is also reflected in a drop of heart rate signaling a close correlation between EEG changes and the centrally mediated drive of the heart rate which results in bradycardia, often seen after high dose opioid administration (Figure 46). Such central effects of opioids on EEG activity can be reversed by the specific antagonist naloxone resulting in a dominance of beta activity and an arousal reaction (Figure 46).

Pethidine, morphine, alfentanil, fentanyl, and sufentanil in doses higher than 20, 180 mg/kg or 5, 4, and 4 mg/kg

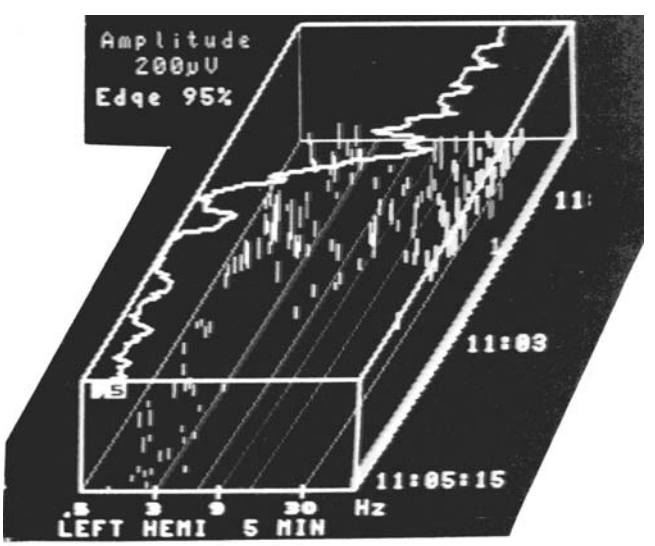


Fig. 45. Effect of 0.3 mg of fentanyl i.v. on EEG power spectra in a premedicated patient for the induction of anesthesia. Shortly after the injection there is a marked decline of fast beta- and aIpha- and a dominance of delta-activity followed by a reduction in the activity edge as low as 0.5 Hz. The latter indicates the point at which 95% of aIl the electrical activity resides. Activity of the brain as it is analyzed and processed by the Lifescan™ EEG analysis system and then displayed in one grid. Amplitude gain 200 µV.

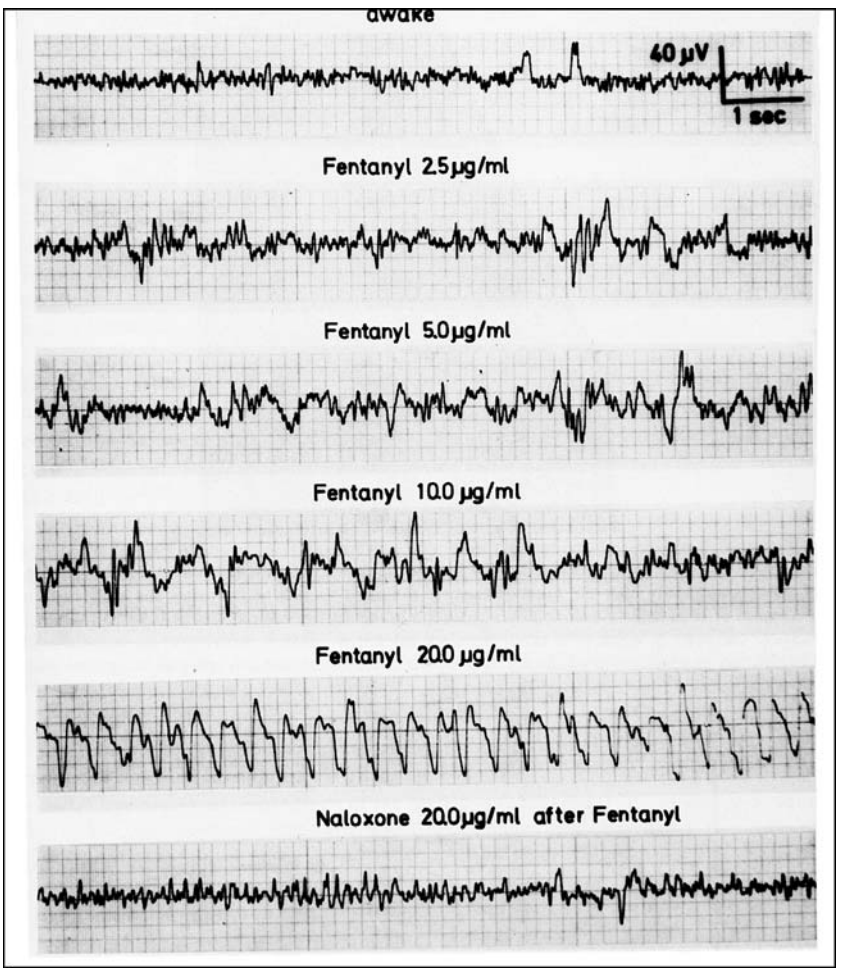


Fig. 46. Dose-related increase in slow wave activity of the EEG during fentanyl perfusion of the IVth cerebral ventricle in the canine and its reversal by the subsequent perfusion of naloxone. The data suggests that the ARS is the primary site of the sedative action of opioids affecting cortical activity (adapted from [51]).

respectively have been shown to produce convulsions in the canine [52]. As such massive doses are never used in man, no such effects will be observed. The clinical effect of the short acting opioid alfentanil and remifentanil on the EEG can be used to evaluate the onset of opioid activity when compared with fentanyl or sufentanil. A representative example of the plasma concentrations of the corresponding opioid and the central nervous effects as demonstrated in spectral edge frequency of the EEG is shown in the figure.

Patients received either alfentanil 1500 μg/min, remifentanil 150 μg/min, fentanyl 150 μg/min and sufentanil 15 μg/min over a period of 5 min. With alfentanil and remifentanil the onset of effects was 1.1 min, demonstrating that spectral edge closely correlated with serum concentration. With fentanyl and sufentanil onset of effects was 6.45 and 3.5 min respectively, with spectral edge changes lagging behind serum concentrations [53]. All opioids of the fentanyl series (i.e. alfentanil, fentanyl, sufentanil and remifentanil) cause similar EEG changes, characterized by progressive slowing in frequency and increase in amplitude with increasing dosages (Figure 47). Maximum effect is characterized by a dominance of delta waves with slow frequency and large amplitude. Although the reliability of the EEG as a measurement for correlation of dose with clinical effect has not yet been established, its potential use has thus been demonstrated, showing a relationship between plasma levels and drug effect with opioids used in anesthesia [54, 55].

The central action of mixed agonist/antagonists such as nalbuphine or butorphanol can be demonstrated in the change of EEG power spectra. Due to their antagonistic

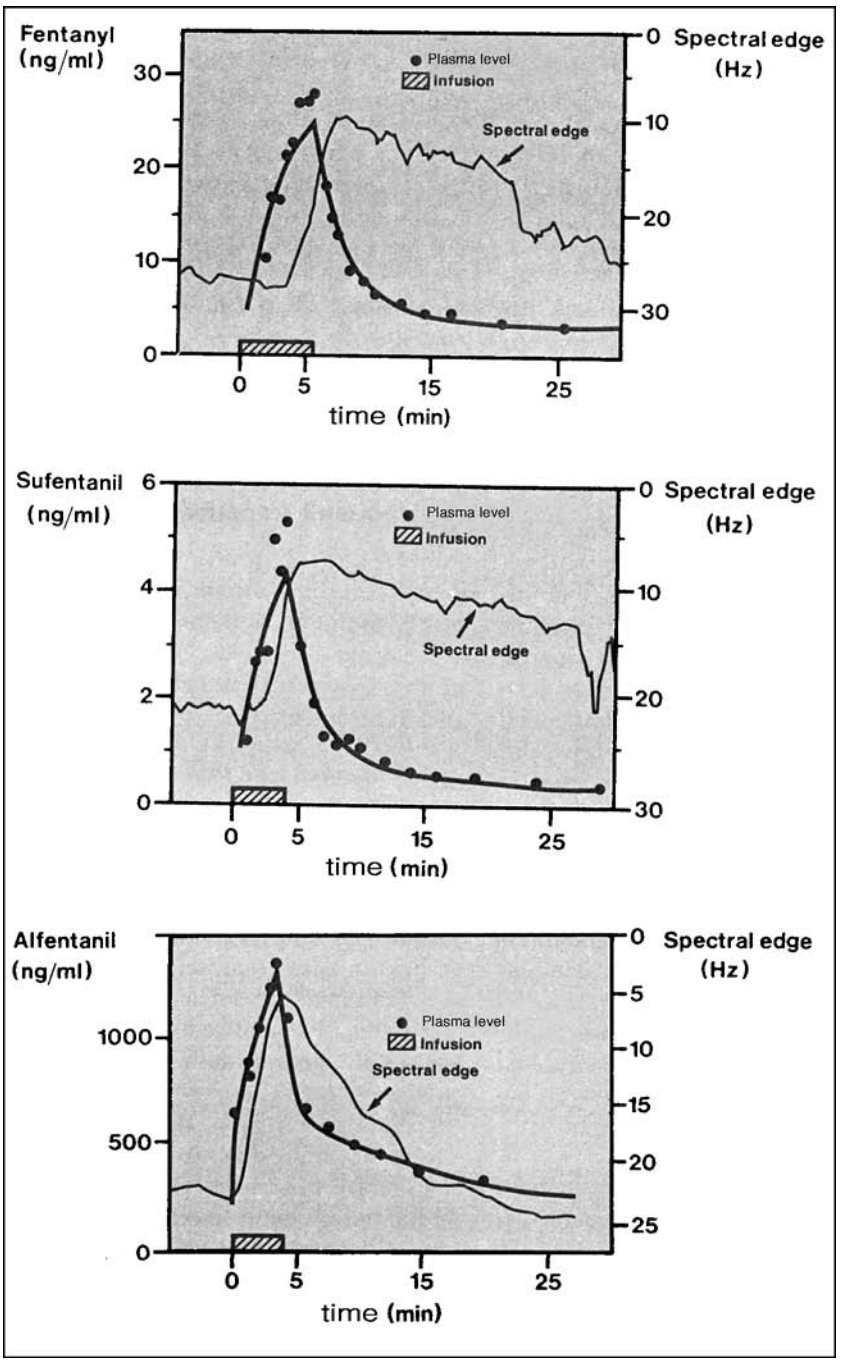


Fig. 47. Change of spectral edge frequency and of serum concentration after fentanyl, sufentanil and alfentanil infusion respectively. The faster decline of spectral edge frequency after alfentanil reflects a faster elimination of the compound from the CNS and a faster recovery from the anesthetic. Note, the close correlation of spectral edge and plasma alfentanil-levels (adapted from [56]).

potency these compounds are able to reverse some of the effect of an overhang induced by the previous opioid ligand such as fentanyl resulting in an increase of vigilance (Figure 48).

Tramadol

The effect of tramadol, which is a weak narcotic analgesic, on the EEG demonstrates a totally different picture than any

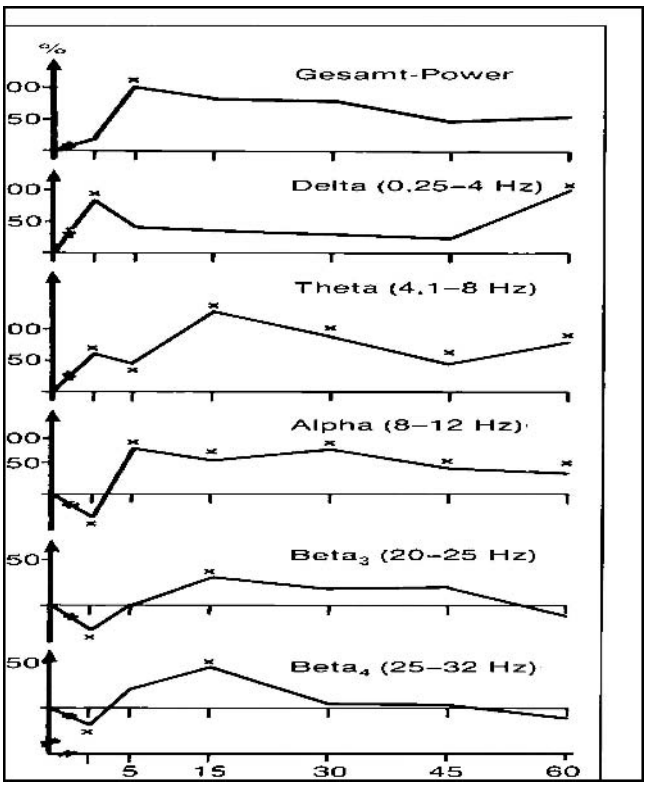


Fig. 48. Summary of effects of the mixed agonist antagonist on patients after opioid-based anesthesia, resulting in a reduction of power in the delta- and an increase of vigilance as reflected in the significant increase of power in the alpha- and beta-domain. Adapted from [57].

of the other opioids-like agents. When given in increasing concentrations (50, 100 mg) to elderly patients who were in need of an analgesic because of chronic osteoarthritis pain. There was a dose-related decrease in the delta- with a concomitant increase of power in the fast beta- and alpha-domain (Figure 49).

This increase in vigilance also was associated with a reduction in depressive mood, displeasure and an increase in cooperative behavior. As to the mode of action it was suggested that tramadol, in addition from its interaction with the opioid receptor, acts as a monaminergic reuptake inhibitor, which results in an increase of noradrenaline, dopamine and serotonin at the synaptic cleft of the aging brain. A similar desynchonisation effect is seen during anesthesia when this opioid is given as an intravenous dose on-top a volatile agent [59].

Benzodiazepines

Benzodiazepines, in a dose as they are used for preoperative anxiolysis, have some effect on the EEG which is characterized by an increase in alpha activity (=synchronization) with resultant sedation. However, after the administration of high doses as used for induction of anesthesia with midazolam or diazepam, in the EEG, contrary to all the other induction agents, demonstrate an increase in fast EEG activity of the beta-band, which reaches its maximum when the patient is asleep (Figure 50). Such an increase of beta waves in the EEG is a characteristic trait of all benzodiazepines; those with a more hypnotic component in addition will accentuate delta-activity [60].

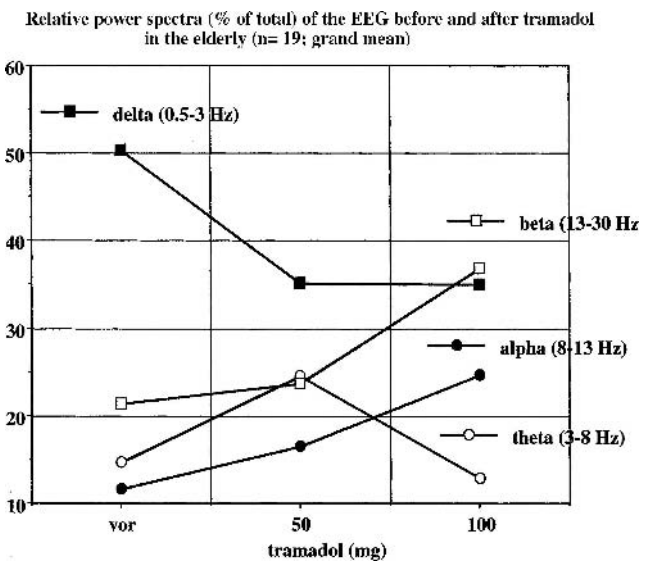


Fig. 49. The effect of increasing doses of tramadol on EEG power spectra in elderly patients (>70 years) [58].

Propofol

Similar to the effects of benzodiazepines can also be observed when the pure hypnotic propofol is given for the induction of anesthesia (2 mg/kg). The increase of activity in the beta-range of the EEG coincides with unresponsiveness of the patient. This suggests a similar effect of benzodiazepines and propofol (Figure 50). Due to its high lipophilicity, the compound rapidly passes the blood brain barrier and induces its central effect. Thus, when benzodiazepines and/or propofol are used, the depth of anesthesia does not correlate at all with the shift of power into the higher frequency range. Similar as in benzodiazepine administration, once N_2O is added, maximum power is shifted to the alpha-band [61].

Ketamine

The agent ketamine, which is used in dissociative anesthesia and in emergency medicine for analgesia, and sometimes

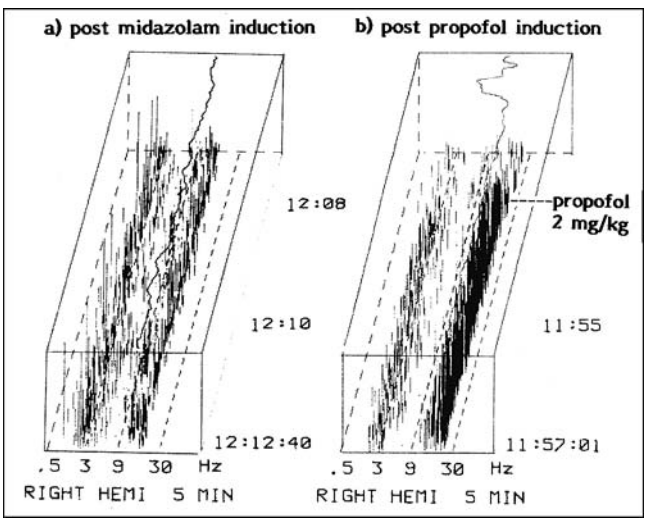


Fig. 50. Characteristics of power spectra and the corresponding spectral edge in the fast alpha to beta range as a result of the injection of midazolam 15 mg (left) and propofol 2 mg/kg respectively (right) used for the induction of anesthesia. When N_2O is added, the latter results in a shift of power in the lower frequency range.

also is part of a sedative regime in the ICU, induces a marked increase in the theta-band of the EEG. After a normal dose of 1–2 mg/kg of ketamine the EEG consists of a mixture of 5–6 Hz, moderate high amplitude activity with very fast 30–40 Hz short amplitude waves superimposed. With high dosages such as 2–4 mg/kg, spike wave complexes can occur which, with further increase, result in generalized seizure activity [62, 63] when the agent is given as a sole anesthetic. Such increase in cortical activity purportedly is linked to a pro-convulsive action in the limbic and thalamic region [62]. The increase in theta-activity is pronounced when the more selective stereoisomer S (+)-ketamine is given and lower concentrations results in a similar theta-activation as the racemic mixture [64, 65].

Detecting cerebral ischemia in cardiopulmonary bypass

Neurological complications are common after complex aortic reconstruction. Therapeutic opportunities for interventions to prevent neurologic injury during these types of operations are possible, but require the ability to assess continuously neurologic function during general anesthesia. Electroencephalography (EEG) permits the continuous online detection of neuronal ischemia. Intraoperative EEG monitoring during aortic reconstruction can detect cerebral malperfusion upon initiation of extracorporeal circulation, diagnose cerebral hypoperfusion caused by an inadequate arterial pressure, and provide physiologic criteria for optimal cerebral metabolic suppression during deliberate hypothermia for circulatory arrest. Immediate detection of neurological events enables the surgeon, anesthesiologist, or perfusionist to intervene to prevent complications. The relationship between EEG activity and the adequacy of cerebral blood flow has been well demonstrated for carotid endarterectomy. Decreased cerebral blood flow producing cerebral ischemia causes changes in the EEG within seconds. Although the EEG has been used for many years, early attempts to demonstrate a benefit for routine cardiac surgical cases have been inconclusive. In order to demonstrate efficacy, a diagnostic monitor must provide information in a timely fashion and assess the outcome of therapeutic interventions. For example, EEG monitoring would have little impact in routine cardiac operations where neurological dysfunction is primarily caused by cerebral emboli and outcome is unlikely to be affected by clinical intervention after the event. In contrast, the onset of abnormal, EEG activity during aortic reconstruction indicates acute cerebral malperfusion that can be corrected surgically or by changes in circulation management. Because there is greater risk of neurological complications with aortic surgery. EEG monitoring should have a greater potential for improving clinical outcome. The event associated with the greatest risk for cerebral malperfusion in patients undergoing complex aortic reconstruction is the termination of cardiac output with the onset of cardiopulmonary bypass (CPB). The consequent alteration in the pattern of blood flow in the aorta can reposition the intimal flap in patients with aortic dissection thus causing ostial obstruction of arch vessels leading to cerebral ischemia. On more than one occasion, unilateral EEG slowing has detected and averted malperfusion of the right carotid artery caused by a dissection of flap obstructing the innominate artery with the onset of CPB.

In several situations, the detection of acute global EEG slowing detected insufficient aortic blood flow in the true lumen that was created by inadvertent CPB perfusion via the false lumen that had a relatively intact intimal layer.

Immediate detection averts a disastrous outcome by prompting the surgeon to open the aorta and fenestrate the intimal flap permitting perfusion of the cerebral vessels. On the other hand, in less acute conditions, generalized EEG slowing may represent hypoperfusion caused by unrecognized cerebrovascular disease and often improves in response to pharmacologic interventions to increase the arterial pressure. The ability to detect and treat intraoperative cerebral hypoperfusion using EEG may not only decrease the risk of stroke, but may decrease the risk of postoperative neurocognitive dysfunction.

Circulatory arrest is often required in operations performed on the aortic arch. The only proven neuroprotective strategy for circulatory arrest is deep hypothermia to decrease cerebral metabolic requirements.

There is no consensus as to the best temperature or cooling duration for the conduct of circulatory arrest. Further, no peripheral site exists to accurately measure brain temperature. EEG monitoring provides a physiologic indicator of the effects of hypothermia on the brain. The cessation of EEG activity or electrocortical silence during deliberate hypothermia has been advocated as a means to detect the adequacy of cerebral metabolic suppression for circulatory arrest. Body temperatures during active cooling are not reliable indicators of hypothermic-induced changes in brain function.

No single site or combination of sites consistently predicted electrocerebral silence.

Several studies have found that there was substantial variability from patient to patient in the absolute temperature and time to achieve electrocortical silence.

In a prospective observational study, the total cooling time required to achieve electrocortical silence was dependent on several factors including hemoglobin concentration, arterial carbon dioxide tension, and cooling rate. The temperature required to achieve electrocortical silence ranged from 12.5 °C to 27.2 °C and had a median value of 18 °C. Therefore, cooling to a set temperature would be expected to produce non-uniform levels of cerebral protection compared to cooling to a specific a physiologic endpoint, such as electrocortical silence. Cooling patients to 18 °C would have failed to establish electrocerebral silence in 50% of the patients, potentially increasing their risk of postoperative neurological morbidity. Conversely, cooling all patients to 12 °C would have needlessly subjected some patients to the inherent risks of excess hypothermia or prolonged CPB.

Opponents to the routine use of EEG monitoring for complex aortic operations argue that electrical artifacts and "nonspecific changes" limit one's ability to interpret the EEG in the operating room. Improvements in instrumentation and the elimination of electrical artifacts caused by the roller pumps of the bypass machine by the use of centripetal flow pumps have improved the diagnostic capabilities of intraoperative EEG. By recognizing the suppressive effects of general anesthetics on the EEG, one can increase its diagnostic potential by maintaining a stable anesthetic state.

Presently, the most significant contribution EEG monitoring can make to patient care, is that of the early detection of cerebral dysfunction, especially that is due to ischemia. Several possible causes of reduced cerebral oxygen delivery are shown in the following table. Since functioning of the cerebral cortex is extremely sensitive to any paO_2 changes, an insufficient cerebral blood flow or inadequate partial oxygen pressure, this is reflected within seconds in the EEG and/or the evoked potential (Figure 51) [66–68] (Table 3).

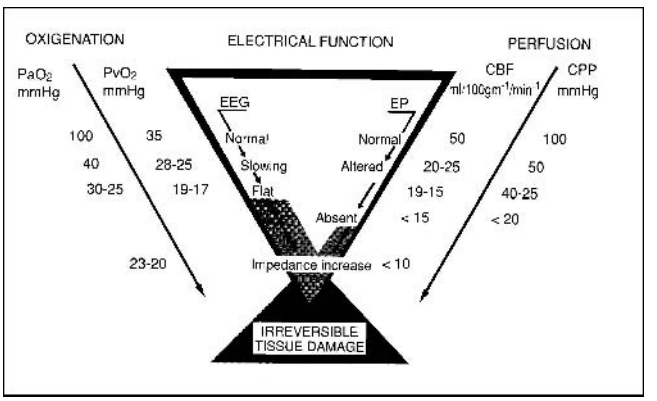


Fig. 51. The changes in brain electrical activity following a decrease in blood oxygenation and/or, a decrease in cerebral blood flow (CBF) with concomitant reduction in cerebral perfusion pressure (CPP). PaO_2 = arterial oxygen tension; PvO_2 = mixed venous oxygen tension.

The typical pattern in the EEG seen during cerebral ischemia is:

1. Reduction or loss of high frequency (Figure 52),

Table 3. The various reasons for a loss in cerebral activity of the EEG

Factors reducing oxygen delivery to the CNS

1. Decreased oxygen-carrying capacity:
   - Anemia
   - Hypovolemia
   - Carbon monoxide poisoning
2. Decreased arterial oxygen content:
   - Decreased inspired oxygen (hypoxia mixture)
   - Inadequate ventilation (disconnection, malfunction)

Factors decreasing cerebral perfusion pressure

1. Decreased systemic arterial pressure:
   - Low blood volume
   - Low cardiac output (pump failure, aortic clamping, arrhythmias)
   - Blood pooling (high dose opioids, nitroprusside, nitroglycerin)
2. Increased intracranial pressure:
   - Hypercapnia
   - Acute systemic hypertension
   - Mass lesions (hematoma, tumor, ruptured aneurysm)
   - Post head injury with edema
3. Mechanical obstruction of cerebral vessels
   - Thrombus
   - Embolus - air (on occasion)
   - Surgical clamping of carotid artery
   - Vasospasm

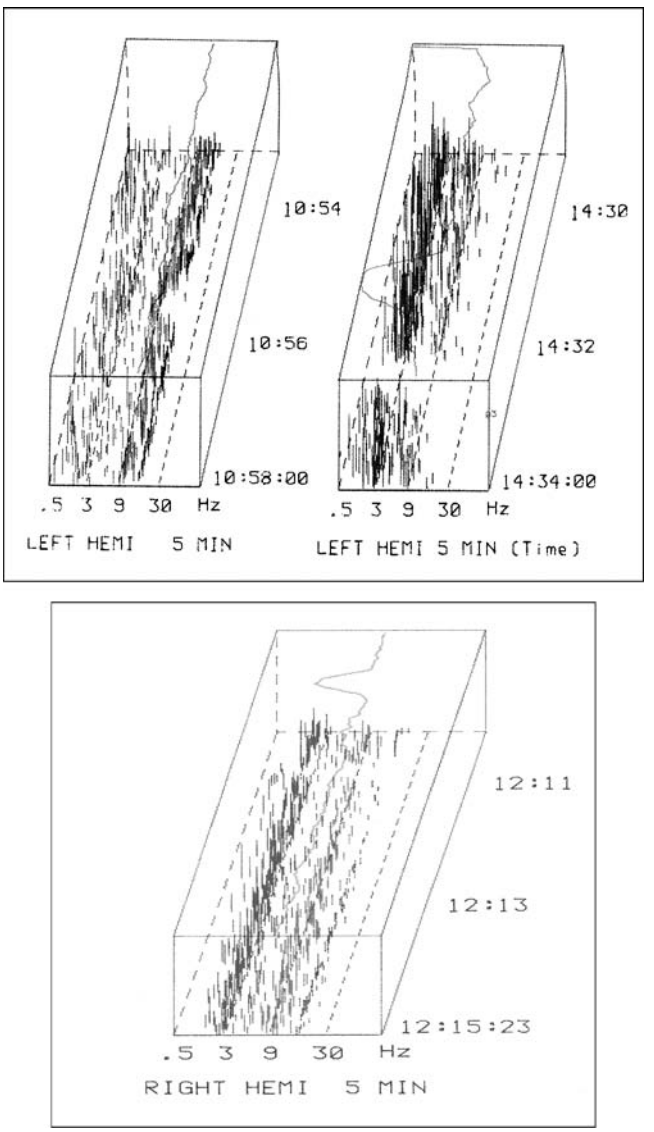


Fig. 52. Representative examples of patients on ECC (extracorporeal circulation) where temporary stop of the pump for only three seconds results in a temporary loss of fast EEG activity as visualized in the marked reduction of Spectral edge frequency (red line).

2. Appearance of large amplitude slow waves in the delta range,
3. Prolonged ischemia eventually results in a decrease of amplitude and frequency leading into isoelectricity.

Even a local decrease in cerebral blood flow, as it occurs in a cerebral embolus results in an EEG change which may even become visible in the spectral analysis of the EEG recorded some distance away from the anatomical site of ischemia [66]. This is mainly due to the fact that computer analysis is more sensitive to changes in the high frequency pattern than normal interpretation.

The EEG appearances of any ischemic episode are similar. Differentiation are made by closely observing the clinical situation and focusing on:

(a) blood pressure,
(b) ECG,
(c) oxygen saturation,
(d) surgical maneuvers, and
(e) drugs being administered.
Other concurrent factors, which alter the intraoperative EEG, are:
(f) change in the depth of anesthesia,
(g) temperature changes (controlled hypothermia), and
(h) changes in CO_2 content.

The latter, however, may only be recognized by their relatively slow onset lasting for several minutes as opposed to changes caused by ischemia, which generally occur within seconds. One should always keep in mind that there are situations where changes in the EEG may occur acutely upon injection of an anesthetic, which due to its pharmacokinetic profile rapidly passes the blood brain barrier.

Such situations may be found in high-dose opioid anesthesia, where fentanyl induces an immediate and marked reduction of fast frequency of the EEG with resultant low frequency and high amplitudes in the delta range (Figure 53). Thus, attention should always be put to the clinical context during which the EEG is observed. Also, it should be noted that a decreased activity with an increase in amplitudes precedes particularly ischemic events of the cortex, whereas ischemia of the capsula interna or the thalamus may result in unnoticeable EEG changes or only in minute alterations in the alpha rhythm in the awake patient. Brainstem ischemia, however, appears in the EEG as a widespread slowing and a decrease in amplitude [69].

Differentiate between ischemia and anesthesia-related EEG changes

Such a differentiation is of clinical importance as it results in a major difference in decision-making, and some of the major points outlining the induced ischemic-related events in the EEG will be summarized as follows:

1. The changes are of focal nature. Since such changes are seldom induced by an anesthetic, they rather relate to intracerebral or cerebrovascular pathology. The situation may however, become more complex when global

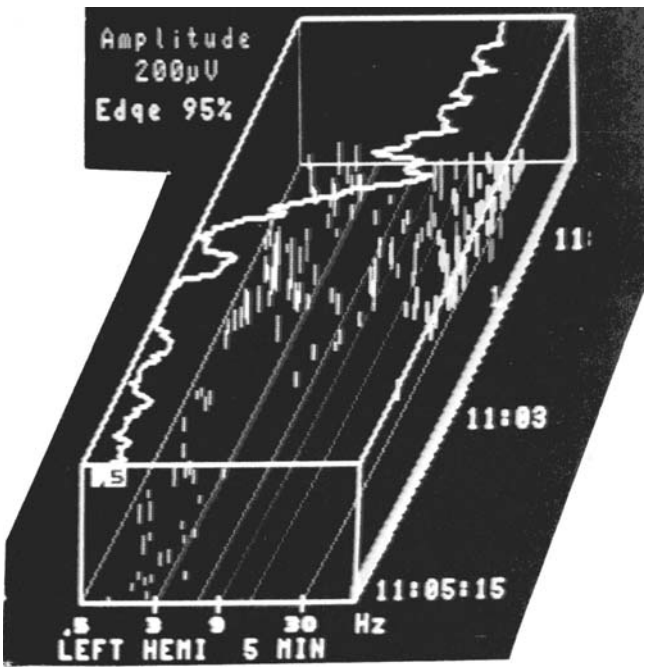


Fig. 53. Example of the sudden drop of EEG activity and a shift of spectral edge activity to the left in a patient who had just received 0.35 mg fentanyl for the induction of anesthesia for CABG (event 1). If no anesthetic would have been given, such a drop is characteristic for malperfusion.

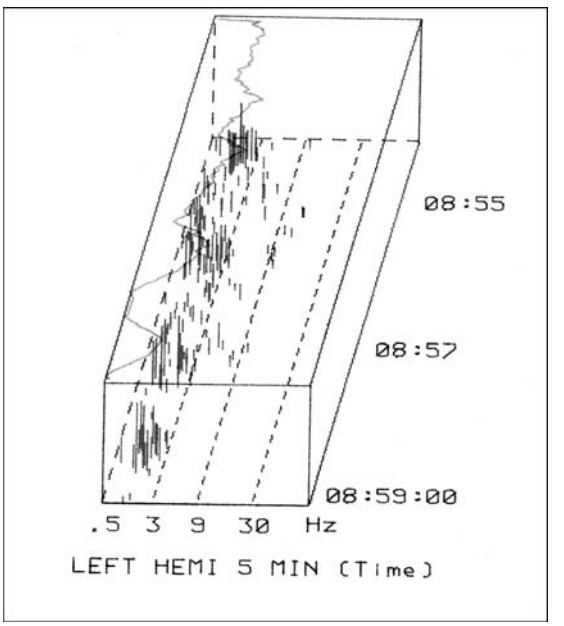


Fig. 54. Representative example of a patient receiving isoflurane-oxygen anesthesia while being on ECC (extracorporeal circulation). Mean perfusion pressure 50 torr. With a core temperature of 25°C. an isoelectric pattern with intermittent slow delta waves develops. The latter is clearly seen in the fluctuating activity edge (EEG power spectra derived with the Lifescan™ cerebral monitor).

hypoxia has to be differentiated from a deepening of anesthesia and/or hypothermia. Yet, the clinical situation and the pattern of the original EEG wave provide important information allowing the determination of the etiology of the EEG changes.

2. The tracings show an isoelectric (flat-line) EEG. Aside from a severe hypoxemia a similar pattern may also be produced by deep hypothermia (Figure 54), large doses of barbiturates greater than those used to induce anesthesia, and high isoflurane concentrations. It is, however, conceivable that neither hypothermia nor barbiturate injection of sufficient magnitude could occur without the awareness of the anesthesiologist.
3. When is there an onset of EEG slowing? The pattern of development of EEG slowing is important, as inadequate cerebral oxygen supply is abrupt, thus slowing the EEG, while deep anesthesia requires time to develop. Thus, the onset of EEG slowing is of a more gradual nature. Hyperventilation may also produce EEG slowing. This, however, is in response to cerebral vasoconstriction as induced by hypocarbia, which in return produces hypoxia of a mild degree. These changes are also abrupt in onset and the coexistence of hypocarbia as an etiology can be determined by blood gas analysis or end-tidal carbon dioxide measurement.

EEG slowing occurs with cardiovascular changes

Excessive inhalation anesthesia results in hypotension, a cardiovascular effect that may occur before, or together with, the EEG changes (Figure 55). The additional change in cardiovascular parameters then provides information of the etiology of EEG slowing. Additionally, enflurane and isoflurane produce burst suppression prior to or with EEG slowing. Ischemia normally does not produce burst suppression.

5. EEG slowing with high dose opioid administration. Injection of potent opioids may also produce an abrupt onset of EEG slowing. This likely would occur at the start of the case and under a situation in which a question about the etiology of the EEG change is unlikely. Severe hypoxia during opioid anesthesia still produces an isoelectric EEG.

In summary, the EEG signal by itself does not allow the determination of the etiology. It is the same as measuring a blood pressure of 80/50, which does not tell whether this drop is due to a loss in volume or vasodilatation. Thus, it is important to simultaneously consider the clinical setting, and as in blood pressure recording, evaluate the EEG in the context of all other clinical parameters. Only then is it possible to make a differentiation of deep anesthesia from hypoxia in EEG monitoring.

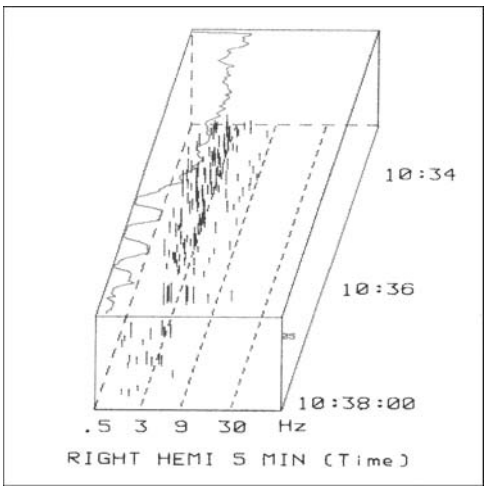


Fig. 55. Representative example of a patient undergoing AC by-pass operation under isoflurane anesthesia. Body core temperature 31°C, and mean perfusion pressure 50 torr. In the EEG there is a gradual loss of activity lasting over 2 min. Only when the pump technician raised perfusion pressure, did EEG activity in the delta band reappear. The patient uneventful recovered from the operation. Time scale on the right hand side.

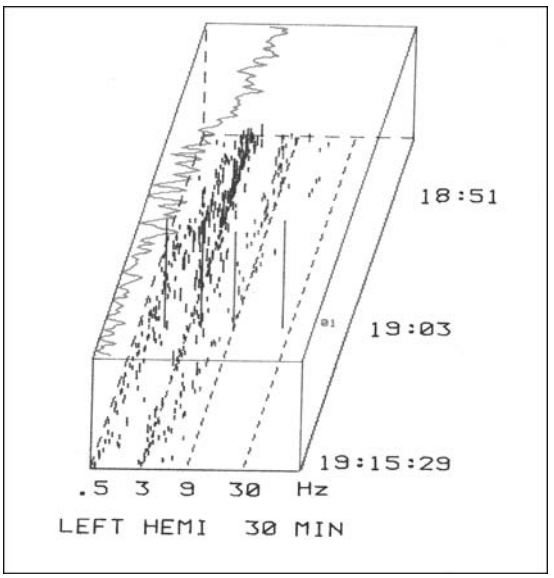


Fig. 56. Example of a patient undergoing cardiopulmonary bypass operation with hypothermia with gradual decrease of body core temperature to 22°C.

Monitoring of the EEG during cardiac surgery

Cardiac surgery provides the best opportunity to demonstrate the benefits of intraoperative EEG monitoring. This is because during cardiopulmonary bypass, the largest number of potentially preventable perioperative brain injuries can arise. This clinical problem also represents a major opportunity for improvement of health care delivery which may demonstrate that in the absence of rapid cooling or anesthetic bolus, the odds are >500:1 that a sudden loss of EEG activity would precede a serious cerebral injury. Univariate (suppression ratio), multivariate (bispectral index) or quantitative EEG descriptors provide a simple method for minimizing unnecessarily long duration of anesthesia and the administration of anesthetics, which eventually would result in slower recovery, a longer stay in the ICU with an increase in hospital costs. When coupled with transcranial Doppler (TCD), and cerebral oximetry, EEG monitoring during cardiac surgery is clearly effective in reducing both complications and costs.

The greatest potential for ensuing CNS damage is during extracorporeal circulation (ECC). This is due to a number of causes:

(a) Sudden hemodilution with the onset of ECC,
(b) Change from palatial flow to non-pulsatile flow,
(c) Reduction in mean arterial pressure (see Figure 56)),
(d) Exposure of blood to foreign material,
(e) An embolic event by loosening of arteriosclerotic material during manipulation at the great arteries, and
(f) Air embolism. [70].

The major reduction of body temperature by itself, although planned, has a dramatic effect on the EEG. Even at stable concentrations of the anesthetic, hypothermia produces progressive slowing in the EEG frequencies in a step-related fashion. Ultimately, there is a reduction in amplitude followed by intermittent suppression, and finally total suppression of all EEG activity, which occurs with rapidly developing hypothermia around 25°C [71]. A representative example in the following figure depicts the various changes the EEG power spectrum will undergo during hypothermia.

In spite of the continuous steady level of isoflurane via bypass into the oxygenator, there is a gradual decrease of frequency and of spectral edge activity (solid line), as viewed in a typical Lifescan™ display on screen. In the 'glass box', results are displayed in a three-dimensional moving picture with the various EEG frequency bands at the X-axis, their corresponding amplitudes at the Y-axis while the Z-axis into the "depth" of the screen reflects time. Note that with deepening of body core temperature burst suppression will occur, which tends to last longer until finally there is a flat processed EEG (Figure 56). These changes are reversed as body core temperature goes up again, resulting in an increase in amplitude and frequency of the EEG. The latter is signified by a shift of the Spectral

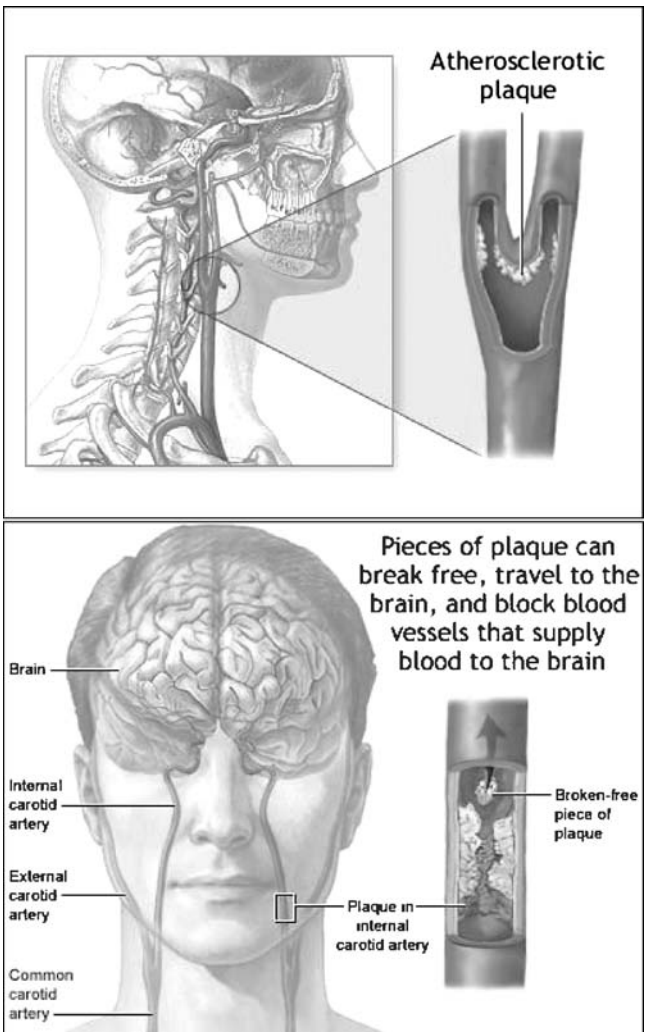


Fig. 57. The major course of carotid occlusion, arteriosclerotic plaques resulting in cerebral malperfusion and a possible functional deficit during CEA.

Edge Activity' from the left (delta band) to the right (alpha band).

EEG monitoring during carotid endarterectomy (CEA)

During carotid cross clamping several factors have to be taken into consideration:

1. Vagal stimulation with carotid retraction—Rx an anticholinergic or put lidocaine on the carotid
2. Heparin (5000–10,000 U) before cross clamping.
3. Shunt may be placed due to neuro/EEG change
4. Keep BP high to perfuse across Circle of Willis
5. Unclamping may result in reflex bradycardia and vasodilatation.

Postoperatively check for neurodysfunction and possible airway compromise.

Carotid endarterectomy (CEA) is now being performed over 100,000 times annually in the United States and other countries. This number is likely to increase due to the aging of our society. Further increase has been prompted by the Asymptomatic Carotid Atherosclerosis Study (ACAS) finding [72] of a 50% risk reduction of ipsilateral stroke in asymptomatic patients with greater than 60% carotid narrowing. A second important conclusion of this study was that surgical benefit to such patients required that the combined incidence of perioperative mortality and morbidity be <3% [73]. The low absolute incidence of neurologic complications in the study population is not representative of national experience. Thus, an onus is placed on surgeon and the anesthesiologist to maintain a low complication rate in order to perform the surgery and/or receive reimbursement. The role of neuromonitoring in helping achieve this goal is highly controversial. Despite a long and often favorable experience with electrophysiological techniques during CEA, reports on their clinical benefit are quite inconsistent. For example, Wober and coworkers [74] used a meta analysis of 3,136 patients from 15 previous studies to examine the effect of somatosensory evoked potential (SSEP) monitoring on CEA outcome. They concluded that SSEP changes were unreliable predictors of neurologic outcome and consequently provided unsuitable criteria for selective use of an intravascular shunt. Although a similar meta analysis has not been performed for EEG monitoring, numerous reports have failed to find benefit [75, 76]. From the perspective of many insurers, hospital administrators and surgeons, these negative reports have erased the impact of the considerable number of positive reports [77–79]. Most importantly, not a single, adequately powered, randomized, prospective CEA outcome study has been performed on any neuromonitoring modality. Absent such results, the controversy is likely to continue.

Two related factors seem largely responsible for the inconsistent results. First, the incidence of clinically significant perioperative neurologic complications of CEA is not high. This relatively low incidence thus requires large sample sizes to legitimately detect real effect on outcome. For example, to detect a valid statistically significant halving of a 3% complication rate with an alpha of 0.05 and 80% power would require random assignment of 3,068 patients to monitored and unmonitored groups. Not surprisingly, the invalid underpowered studies in the SEP meta analysis and elsewhere lead to random results that tell us more about peer review quality than monitoring utility.

Secondly, the source of CEA neurologic complications is clearly multifactorial – both embolic and hemodynamic. These pathologic processes may be initiated at any time from anesthetic induction through post-anesthetic care

recovery. Monitoring only the period of intentional carotid occlusion will inevitably fail to detect some noteworthy and treatable changes in cerebral perfusion. Since the incidence of preventable complications is low, failure to prevent even one injury in each hundred cases may obscure other successes and degrade the apparent cost-effectiveness of neuromonitoring.

The greatest hindrance to widespread use of neuromonitoring for CEA is the cost of personnel, not monitors. Therefore, it makes both clinical and economic sense for the monitorist to do everything possible to prevent a perioperative neurologic complication. Counterproductive and parochial arguments over the relative benefits of electrophysiologic, ultrasonic and near-infrared spectroscopic monitors miss the essential point. To justify the cost of the monitorist, the complication rate must be reduced to zero. The multifactorial etiology of the complications suggests that this may be best achieved with multimodality monitoring of both hemodynamic and embolic processes. Total elimination of complications requires, in part, information only available through TCD (transcranial Doppler) monitoring. Lennard et al. [80] were able to achieve the zero complication goal with the aid of TCD and EEG monitoring. In the EEG bilateral baseline values also identify marked interhemispheric flow asymmetries. Armed with such knowledge, the monitorist may prevent cerebral infarcts resulting from inadvertent arterial compression during neck hyperextension associated with endotracheal intubation or excessive head rotation to achieve maximal carotid exposure.

Multimodal monitoring during CEA using the EEG and transcranial Doppler (TCD)

TCD and EEG monitoring can objectively determine both the need for an intravascular shunt and its proper functioning. Spencer has defined hypoperfusion necessitating shunt placement as a >70% decline in peak velocity below the pre-occlusion reference. Shunt patency may be quantified by the magnitude of velocity increase, once it has been opened. Because most shunts are somewhat flow-restrictive, the velocity typically does not fully return to the pre-occlusion reference value.

Continued surveillance of the TCD and EEG waveform during the entire endarterectomy is essential to ensure adequate perfusion and detect a functional deficit. Unexpected shunt kinking may be rapidly detected and corrected with the aid of TCD and EEG. Even with a patent shunt, hypoperfusion during the endarterectomy may suddenly occur as the anesthesiologist gradually decreases systemic arterial pressure. Controlled hypertension is often used at initial carotid occlusion to facilitate collateral cerebral blood flow. However, this represents a considerable stress to the patient's cardiovascular system. Perfusion pressure decline may suddenly lead to a closure of high resistance collaterals. Thus, TCD and EEG aid the anesthesiologist in objectively determining the lowest adequate perfusion pressure during the critical period of carotid occlusion. In Spencer's series of 500 CEA, hypoperfusion was identified in 16% of the cases.

Post-endarterectomy hyperemia, potentially leading to hemorrhagic stroke, is most commonly seen in those patients with rapidly progressing stenotic lesions. The cerebral vasculature in the affected territory maximally dilates and looses the ability to autoregulate. TCD and the EEG provide a reliable and inexpensive method for detection of this potentially catastrophic phenomenon. Spencer noted that hyperemia, manifested by a doubling of the pre-occlusion reference velocity, occurred in 15% of his series. The small number of patients ultimately experiencing post-operative hemorrhagic infarcts came from this group. The vast majority of these at-risk hyperemic patients were managed successfully with hyperventilation and controlled hypotension.

The source of emboli detected by TCD during carotid dissection and at clamp release is most likely to be atherosclerotic plaque. In these situations, the role of TCD and EEG is to guide the surgeon to technical excellence. The story in the post-anesthesia care unit is quite different. Here, TCD-detected HITS (high intensity signal transients) are almost always platelet aggregates generated by a partially denuded and highly thrombogenic vascular endothelium. If unchecked, these aggregates may mature into occlusive thromboemboli, resulting in infarcts in the succeeding hours or days. Lennard et al. [80] have eliminated all post-operative strokes with the aid of a three-hour TCD monitoring session. They found signs of persistent embolization, characterized by >25 HITS/10 min, consistently preceded injury. Embolization was completely prevented with incremental infusion of the antiplatelet agent, dextran-40.

If TCD and EEG are beneficial for CEA in all these ways, why aren't they used more often? First, in contrast to spectroscopic monitoring, the information obtained is highly dependent on the skill and experience of the monitorist.

In summary, the important role that TCD and EEG monitoring can play in CEA surgery is that:

1. Virtually all neurologic injury associated with CEA is preventable.
2. The sources of this injury are both hemodynamic and embolic.
3. TCD plus EEG is effective in detecting both types of abnormalities.
4. The relationship between EEG activity and the adequacy of cerebral blood flow has been well demonstrated for carotid endarterectomy.

5. Decreased cerebral blood flow producing cerebral ischemia causes changes in the EEG within seconds.

These concepts emphasize the value of TCD plus EEG in responsible multimodality neuromonitoring for carotid endarterectomy.

As to the choice of the anesthetic being used for CEA, no compelling advantage has been demonstrated with either regional or general anesthesia since there was no difference in optimizing perfusion to the brain, minimizing myocardial stress and allowing rapid recovery. The choice is often strongly influenced by the surgeon's preference and the anesthesiologist familiarity with a specific technique, while recent studies advocated, that sevoflurane and/or desflurane anesthesia provided quicker extubation times and recovery profiles after CEA with no significant peri-operative differences in cardiac index and ST segment analysis. Propofol and narcotics in CEA may be associated with hypotension.

Although the relevance of changes in the EEG to neurological outcome after carotid endarterectomy has been challenged [81], reports have outlined the fact that the appearance of transient EEG abnormalities during operation does not necessarily imply a postoperative neurologic dysfunction (Table 4). If intraoperative changes lasted longer than 20 minutes, inevitable consequences would result [66]. The same may hold true when using EEG monitoring to determine adequacy of cerebral perfusion during cardiopulmonary bypass. Even though prolonged isoelectric EEG activity secondary to ischemia does not imply irreversibility, it does, however, imply evidence of ischemia and an immediate danger of tissue damage which should be addressed immediately (Figure 58).

Table 4. Summary of the different modalities advocated for monitoring during CEA

Awake patient	Likely the gold standard for neurologic monitoring. However, there is absence of prospective data that will compel one to choose this method of neurologic monitoring
EEG	Neurologic changes may correlate with EEG. However, there is a fairly high rate of false positives for discriminating ischemia with the EEG
SSEP	Probably not any better than the EEG, but more complex. May be a better indicator of subcortical ischemia
Stump Press	Poor sensitivity and specificity
TCD	TCD may be beneficial for assessing hemodynamic ischemia, shunt function, embolic phenomenon, hyperperfusion syndrome
Oximetry	High false positive rate
JvO2	Sensitivity, specificity and intervention thresholds are not determined

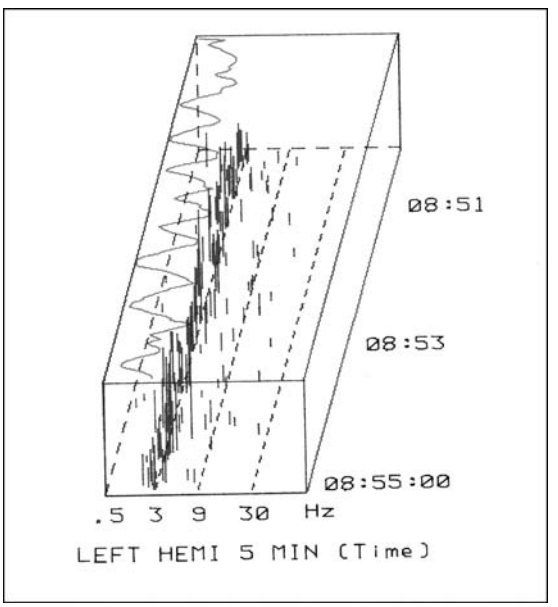


Fig. 58. Change of EEG power spectra and spectral edge activity followed by a drop in body core temperature from 39° C to 22° C in a patient undergoing AC-bypass operation with sequential CEA during isoflurane (1 Vol%) anesthesia. During hypothermia there are periods of burst suppression (electrical silence), which are considered as protective for the brain.

Subtle complications such as impairment of memory may occur after ischemic episodes of less than 10 min. On the other hand, total cessation of cerebral perfusion at hypothermia of 18 °C and an isoelectric EEG will result in no damage, unless this isoelectric episode does not exceed 30 min [82, 83]. Similar effect of a cessation of blood flow to the brain may be observed in carotid endarterectomy. The following changes in EEG power spectra suggest insufficient cerebral blood flow:

1. With the onset of clamping there is a sudden slowing of activity.
2. The drop of EEG activity is related to the side of clamping (side-difference; Figure 59).
3. Once the artery is declamped, fast activity of the affected hemisphere will reappear and if there was no prolonged period of clamping.

CEREBRAL MONITORING IN THE INTENSIVE CARE UNIT

Cerebral monitoring may also be used in the intensive care unit for the same reason as in the operation room, however the following situations now are added:

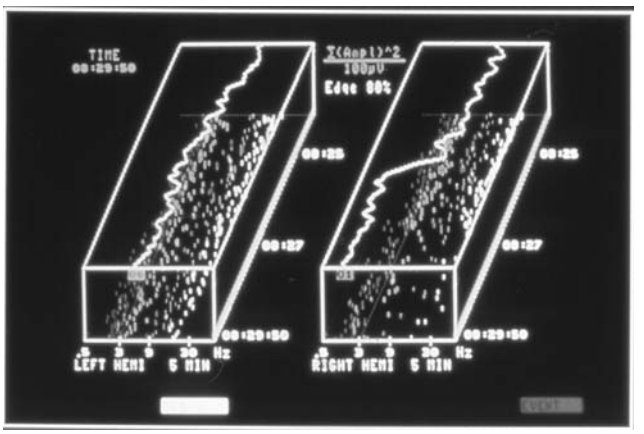


Fig. 59. A typical screen from a patient undergoing CEA with the aid of the Lifescan™ brain activity monitor. On the right hand side there is a sudden shift of the activity edge to the left indicating a decrease in cortical activity while the edge on the left remains constant. A clamp has been placed on the right carotid artery, thus decreasing the blood flow to and the activity of the right side of the brain. If the situation is left unattended, permanent brain damage may result.

(a) As a monitor for epileptic activity in the unconscious patient,
(b) As a dosage guide in the management of barbiturate coma,
(c) As a dosage guide in the management of sedation for tolerance of mechanical ventilation,
(d) As an objective measure in the management of drug intoxication,
(e) As a screening monitor for situations in which "brain death" is suspected, and finally
(f) As a continuous display of cerebral function similar to that of the continuous monitoring of cardiovascular parameters (e.g. arterial blood pressure, central venous pressure, pulmonary artery pressure, pulmonary wedge pressure, etc.).

The following section presents a collection of computerized EEG power traces illustrating the usefulness of applications of EEG monitoring in the ICU. All cases were monitored with the Lifescan™ Monitoring System (Neurometrics, San Diego, USA). EEG power spectra were usually derived from both hemispheres using the electrode montage F_3 and F_4 with the corresponding negative electrode placed on the mastoid A_1 and A_2 respectively. For grounding, the electrode was positioned on the forehead using FpZ.

Monitoring of the CNS following resuscitation

This case represents a patient with obliteration of the left, and narrowing of the right carotid artery after resuscitation (Figure 60). In the EEG power spectrum repetitive seizure activity over the right hemisphere with paroxysmal discharge is reflected in an increase of power in the beta band. As no tonic-clonic muscle activity was visible, epileptogenic discharges could only be made obvious with the aid of the cerebral monitor. The EEG power spectra were useful in several respects:

(a) Localize the site of origin of the epileptic focus (asymmetry between both hemispheres),
(b) Evaluate the efficacy of a therapeutic regime,

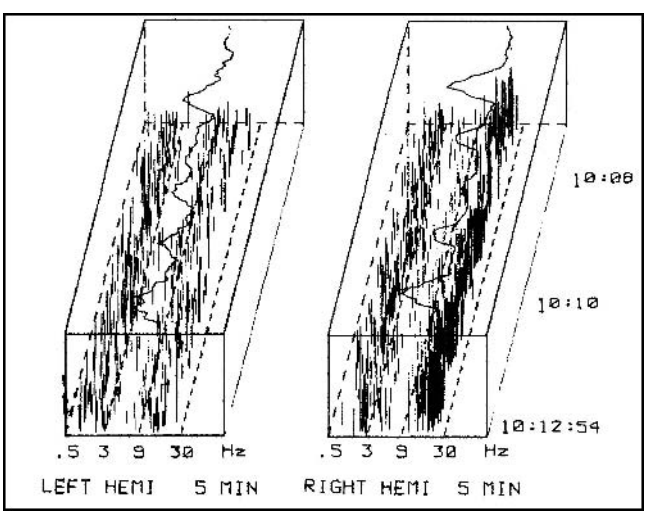


Fig. 60. Representative example of a 68 year old male following resuscitation with resultant epileptogenic activity originating in the left cerebral cortex. In the EEG power spectra epileptogenic activity results in fluctuating power peaks in the fast beta domain. There is a spread of epileptogenic activity to the left hemisphere. The effectiveness of antiepileptic agents was monitored with the aid of the EEG.

(c) Select the individual dose necessary to reduce seizure activity, and
(d) As a follow-up over the next days.

Over the left hemisphere the spread of seizure activity (i.e. increase of power in the beta band) is reduced which suggests that the source of seizures is on the right hemisphere.

Monitoring the comatose patient

Monitoring of the comatose patient is a situation where continuous recording of an EEG should be the standard of care in the ICU. EEG recording at repeated intervals can help with broad diagnostic categorization. In addition, special situations for example monitoring the effectiveness of an epileptic treatment in a head trauma patient, is deemed obligatory. And in the light of other neurological assessments, like the integrity of brainstem reflexes, the age of the patient and the overall clinical picture, it is important to repetitively test the reactivity of the EEG. This especially holds true even in the century of routine computer tomography, which can only give a temporary and anatomical picture of the cerebral status. It however in no way is able to indicate viable neuronal structures or suggest metabolic disturbance due to liver dysfunction or the accumulation of toxic substances with triphasic waves in the EEG. In addition the patients prognosis including a reactive burst suppression pattern, is a good sign, and one can assume that certain arousal functions and sensory systems are working. In such situations, where the brains seizure activity and the cardiac problems are under control, there is good potential for brain function recovery. Such a situation is presented in the following figure, which shows the EEG power spectra of a 42 year old patient who was involved in a car accident suffering from multiple fractures of arms and legs, with a third degree head trauma. Partial tetraparalysis with flaccid paralysis of the left arm was evident. Computer tomography (CT) revealed no signs of intracerebral or subdural mass bleeding. The power spectra showed a pathological slowing of EEG waves over the right hemisphere. Over the left hemisphere fast activity in the beta domain was seen, reflecting a fluctuation of vigilance. The latter is visualized by changes in the spectral edge.

The advantage of computerized cerebral monitoring in such a case is obvious when answers to the following questions are contemplated:

(a) Is there an interhemispheric difference of activity?
(b) Is there any deterioration of cerebral activity over the past 24 h?
(c) What is the effectiveness of the therapeutic regime?
(d) Has there been any sign of epileptogenic activity, which demands an early intervention with antiepileptic agent?

The EEG following cerebral malperfusion

An example in a 75-year-old male who developed hypovolemia postoperatively after desobliteration of the femoral artery, demonstrates irreversible cortical cell damage. His medical history reveals a multiple vessel sclerosis with transient ischemic attacks (TIA). He is in a comatose state, and on nociceptive stimulation synergism of the left arm is more pronounced than on the right side. In the EEG power spectra a marked reduction of alpha to beta activity over the right fronto-temporal with pathological slow waves in the delta-range are derived (Figure 61). Due to the past history, the incidence of acute hypovolemia and the present slow waves, encephalopathy is diagnosed with signs of a right-sided deceleration.

The latter case demonstrates that, in addition to neurological exploration, the EEG power spectra are helpful in many respects:

(a) They provide insight information of pathological EEG activity of the whole cortex,
(b) Give an idea in regard to the prognostic outcome, and
(c) Will show up any sudden deterioration in cortical activity.

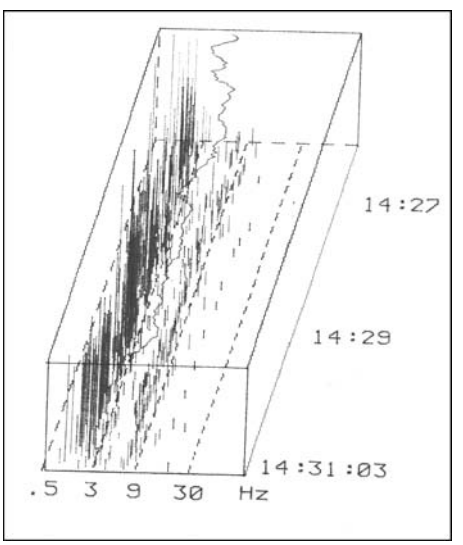


Fig. 61. Sequelae of acute malperfusion in a patient with previous borderline cerebral perfusion. Marked right-sided pathological slow waves suggest damage of cortical structures.

Sedation in the intensive care unit

One of the major concerns in the intensive care situation is the question of how to sufficiently sedate the patient who is on the ventilator, avoiding any overhang of sedatives when the patient is ready to be weaned off. In such a situation the EEG power spectra may become useful as they give an idea about the degree to which sedatives depress the cortex. Deep sedation usually is accompanied by a loss in fast activity in the beta and alpha domain. Doses can thus be tailored individually in order to guarantee a sufficient level of sedation and at the same time avoid a potential overdose. As most regimes, which are used for sedation in the ICU, cannot be judged by the reaction of the cardiovascular system, it is only logical to look at that organ which is considered the target of any sedative, the CNS. The following figure shows the mean effect of sedation using the short acting opioid alfentanil given together with the benzodiazepine midazolam administered via a motor-driven pump to patients who are in need of artificial ventilation. It can be seen that high perfusion rates induce a depressive effect on the fast power spectra with a concomitant dominance of power in the slow delta-domain (Figure 62).

There is a close correlation of power in the alpha- and especially the beta-domain with a reduction in dose during the weaning period. Thus, EEG monitoring during any type of sedation in the ICU setting:

(a) Is a useful tool to guide the clinician in adjusting to the individual dose necessary for tolerance of ventilation,
(b) Is the only way to avoid drug overhang in the weaning period,
(c) Immediately notifies the clinician on the efficacy of the drugs used for sedation,
(d) Is more reliable than any sedative score used in the ICU (for instance Ramsay score)
(e) Gives early warning on the possible development of tolerance during long-term administration of agents, and finally
(f) Results in cost savings because of a reduction in ventilatory time and a reduction of stay in the ICU.

EEG power spectra following mitral valve replacement

Use of cerebral monitoring in the ICU for the preservation of cerebral function is outlined in the following case. A patient in the ICU who had undergone mitral valve replacement, in spite of anticonvulsant therapy still experienced seizure activity with clonic movements of his left side. Due to clonus of the left leg, artifacts are marked by the computer analyzing the EEG waves (Figure 63). The seizure activity was of short duration spreading over to the left hemisphere. At 10.51 a.m. (event 01) muscle activity is evident, which is reflected in the appearance of fast activity with high power, first seen on the right hemisphere and later spread to the left side. Additional therapy with a barbiturate sufficiently depressed muscular jerks. However, in the EEG, high power in the beta domain still reflects abortive seizure activity. Thus, monitoring for the evaluation of effectiveness of drug therapy suggests insufficient dosing. If the patient had not been monitored on a continuous base, abortive seizure activity would not have been noted. As continuous seizure activity results in an increase in cerebral metabolic rate and an increase in cerebral oxygen consumption, damage of borderline nerve cells might ensue.

Focal activity of seizures may look different when a number of anticonvulsants are already on board, which however do not completely abolish hyperactivity in a circumscribed cortical area. This is demonstrated in another patient who after mitral valve replacement developed seizures. With appropriate treatment seizures completely disappeared. In the EEG power spectrum, however, seizure activity is still apparent in the right hemisphere (Figure 64). The hyperactivity is visualized in the "glass box" derived by the Lifescan^{TM} cerebral monitor where a fluctuation of power is reflected in the spectral edge. No such increase in spectral edge is seen in the power spectra of the left hemisphere. lnsufficient anticonvulsant therapy was diagnosed and the dose increased as indicated by EEG monitoring.

In cases of epileptogenic activity, EEG power spectra have helped in the evaluation of sufficient dosing in a patient with tonic-clinic movements. The EEG therefore is:

(a) an indicator when to reduce the dose,
(b) an indicator when to increase the dose,
(c) able to indicate the ineffectivity of a specific anticonvulsant,
(d) able to indicate the efficiency of a combination of drugs, and
(e) an aid in evaluating the severity of seizure activity in the long run.

Use of EEG power spectra in the detoxification unit

Another case reflects the advantage of cerebral monitoring in the emergency and/or detoxification unit where comatose and unconscious patients, due to drug overdose, are treated. The brain as the prime target of centrally active drugs should be monitored similar to any other organ,

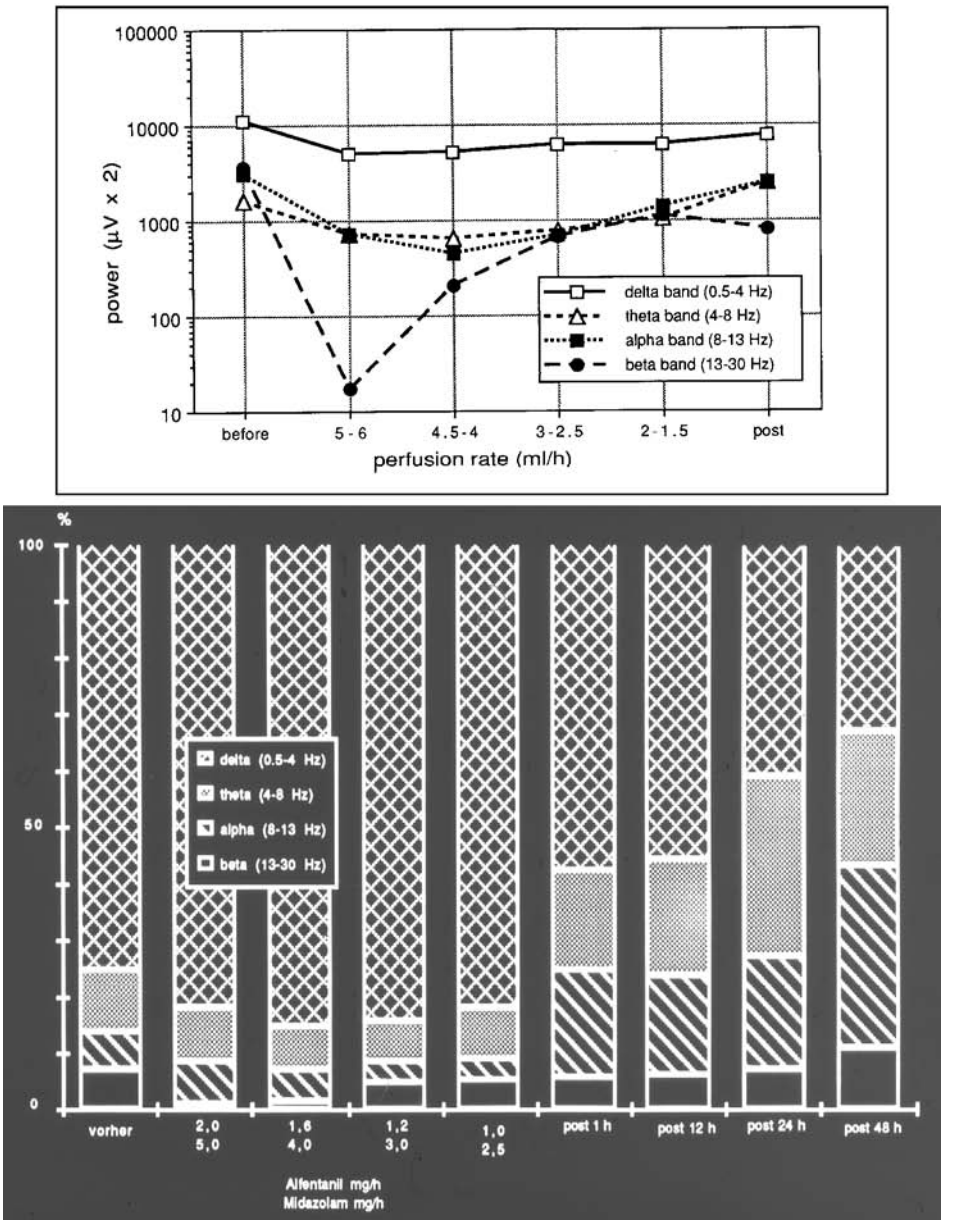


Fig. 62. Change of power in the various frequency bands during the administration of different amounts of an alfentanil/midazolam mixture given to patients ($n = 10$) for sedation in an ICU setting who are in need for mechanical ventilation. Note that the fast frequency beta-band reflects the dynamics of both drugs on CNS activity.

which is at risk in such a critical situation. A 28-year-old female was found in a comatose state in the downtown area. Due to several bruises and lacerations on her head, which raised suspicions of rape, she was taken to the emergency unit. Benzodiazepine intoxication was also suspected as an empty package of flunitrazepam (40 mg) was found in one of her pockets. Computerized tomography and careful neurological exploration revealed no signs of an intracranial lesion.

Blood gas analysis at that time revealed a paO_2 of 44 and a $paCO_2$ of 46 mmHg. Due to deterioration of respiration she was intubated and ventilated with pure oxygen. Blood gas analysis now showed a paO_2 of 356 and $paCO_2$ was 42 mmHg. As intracranial lesions still could not be ruled out and in order to evaluate cerebral activity, she was monitored with a computerized EEG analyzer. EEG power spectra revealed a dominance of activity in the alpha and theta bands with little pathological delta waves

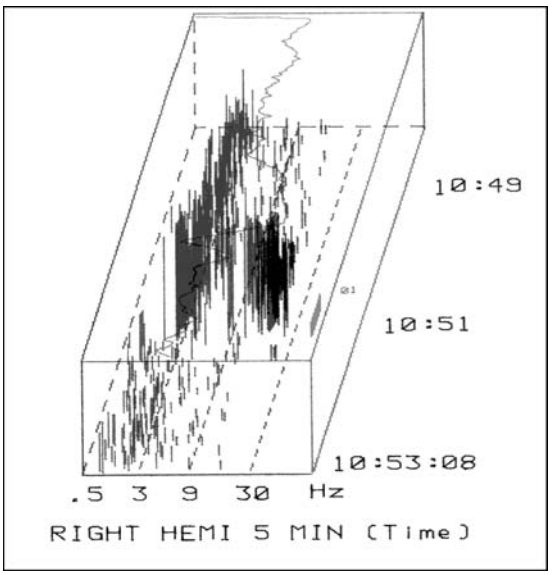


Fig. 63. EEG power spectra of a patient developing seizures after mitral valve replacement. Although the injection of a barbiturate results in the cessation of tonic-clonic movements, the EEG spectra still demonstrated seizure activity, suggesting insufficient dosing.

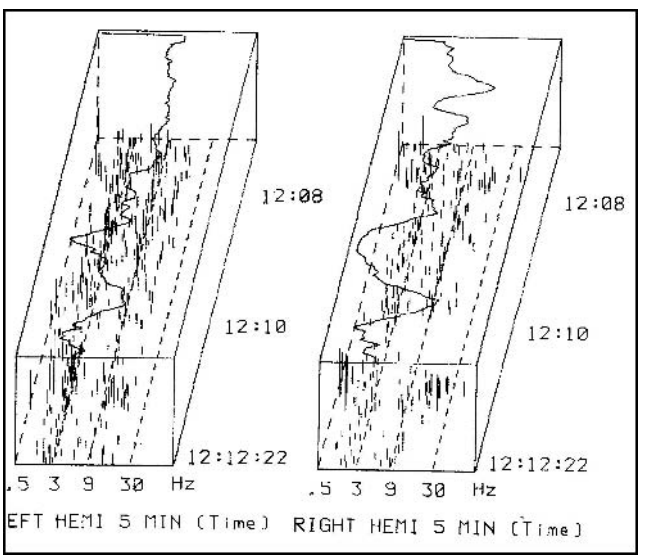


Fig. 64. Another patient after mitral valve replacement with general seizure activity where anticonvulsant therapy induces a suppression of the hyperexcitatory state of the cortex. An active focus however, can be derived from the marked fluctuation of the activity edge in the chrono-power spectra.

(Figure 65). In the EEG a benzodiazepine usually increase fast activity and with a suspected flunitrazepam overdose in mind, the specific benzodiazepine antagonist flumazenil (Anexate^{TM}) was given in incremental doses. The relative power changes, as they were derived from the computed power spectra, showed a marked increase of activity in the

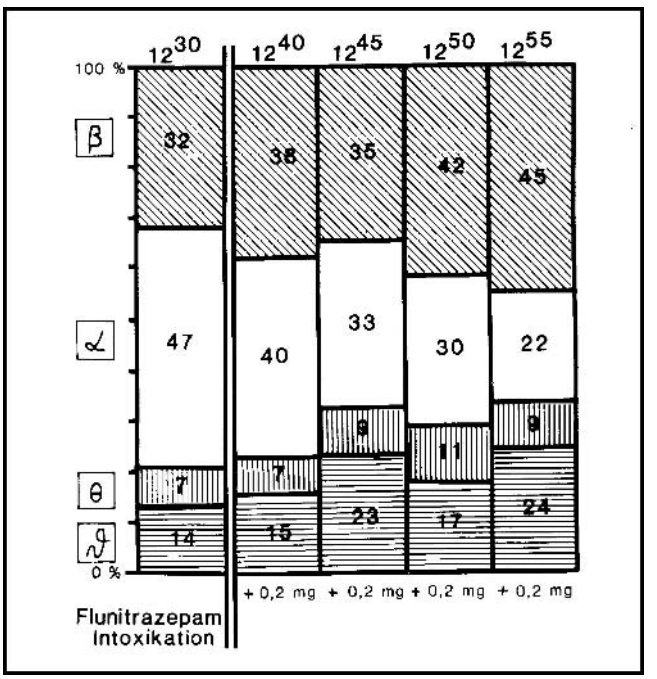


Fig. 65. Relative changes (%) in the various EEG power spectra in a comatose patient with benzodiazepine intoxication receiving incremental doses of the specific antagonist flumazenil (Anexate^{TM}). Recovery of consciousness and increase of vigilance is reflected in an increase in beta-activity.

beta band following the fourth and the fifth incremental dose of the antagonist (Figure 65). Power in the alpha band in the comatose state dropped from a relative value 47% to 22% and beta increased from 32% to a relative value of 45%. These CNS changes reflected the patient's behavior as she slowly regained consciousness, had sufficient spontaneous respiration, did not tolerate the endotracheal tube any more, and after being extubated was orientated to space and time responding appropriately to verbal commands. Blood gas analysis at this time revealed a paO_2 of 67.1 and a $paCO_2$ of 39.6 mmHg with no gross changes in blood pressure and heart rate. While still awake, the patient was sent to the detoxification unit for further surveillance. A rebound of benzodiazepine effect had to be anticipated (shorter half life of the antagonist) and although the patient became drowsy in the next two hours, she could always be awakened, so that ventilatory assistance was never necessary. The case demonstrates that even in the emergency unit cerebral monitoring in certain cases not only is mandatory but may also aid in evaluating the underlying cause of a comatose state. Thus, the following advantages of cerebral monitoring in the above situation can be derived:

(a) An additional, simple and fast aid in evaluating the underlying cause of a coma,

(b) Aid in the treatment of a suspected drug overdose,
(c) An additional instrument to differentiate between an intracranial lesion and central drug effects in an otherwise comatose patient,
(d) A warning signal for resedation and a possible deterioration of CNS function,
(e) A valuable tool for monitoring in the detoxification unit for long term follow up, and
(f) Eliminating the need for ventilatory support.

EEG power spectra to differentiate between drug overdose and brain lesion

The detoxification unit is not only the place where drug overdose has to be treated. In the intensive care unit, especially in cases with long-term sedation, where neurological evaluation of the cerebral status is practically impossible, a drug like the benzodiazepine antagonist in addition to cerebral monitoring can be very useful. This is of interest when the patient has to be ventilated and is sedated with benzodiazepines, and there is the need to differentiate between possible drug overdose and a potential posttraumatic brain lesion. A 60-year-old male with poly trauma and thoracic contusion, had received a total of 3 mg of lorazepam to tolerate postoperative ventilatory support over the past 36 h. Cortical activity, as it was derived from the EEG power spectra (Figure 66), showed a reduction of power in the fast beta band. In order to differentiate between a possible cerebral lesion and drug overdose, the antagonist flumazenil was given in a single dose of 0.2 mg. The antagonist induced a marked increase of power in the beta domain, indicating arousal. This increase in the fast EEG waves could be stabilized by repetitive injections of the antagonist so that the patient could be weaned off much faster from the ventilator. This case demonstrates why cerebral monitoring is useful in an ICU setting:

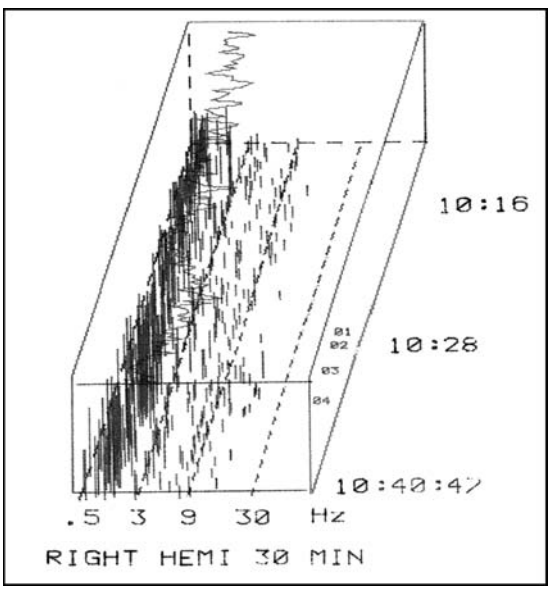


Fig. 66. Patient deeply sedated with a benzodiazepine on respirator therapy. In order to evaluate neuronal response, the benzodiazepine antagonist flumazenil is given. Shortly after the injection power in the beta domain increases suggesting viable cortical structures.

(a) Differentiating between drug overhang and a possible intracerebral lesion,
(b) Adjusting incremental doses of the antagonist, just enough to demonstrate arousal in the EEG, but not too much to induce a sudden awakening with sympathetic overdrive,
(c) Titrating the amount of the antagonist in regard to cortical effects, and
(d) Notifying a possible rebound of sedation which goes hand in hand with decay in cerebral activity and a decay of other vital functions such as respiration.

The "diagnostic window" to the brain during long-term sedation

In certain situations during sedation of a ventilated patient, neurological exploration is necessary. Due to the agent-related CNS depression this is not possible. In such cases the use of a specific antagonists during on-line EEG analysis is a valuable tool to evaluate cerebral function by "creating a diagnostic window" into the sedative regime without total reversal of sedation. Such a "diagnostic window" is characterized by an increase in fast activity in the beta and alpha domain in the sedated patient. Such a "window" is demonstrated in the following figure, since deep sedation is partially reversed with the aid of the specific antagonist. As the half- life of that compound is of short duration, sedation becomes dominant again after a few minutes, suggesting a reactive and viable, not severely traumatized cortex. This reflects one of the few techniques to estimate cerebral activity, a technique which otherwise is impossible in a sedated patient (Figure 67).

EEG power spectra to differentiate between head trauma and drug overdose

Thus, the pharmacological tool in conjunction with automated EEG analysis is useful in all cases of inadvertent overdose of a sedative. The following figure represents the case of a 22-year-old male who had been involved in a motorcycle accident. During diagnostic exploration he had

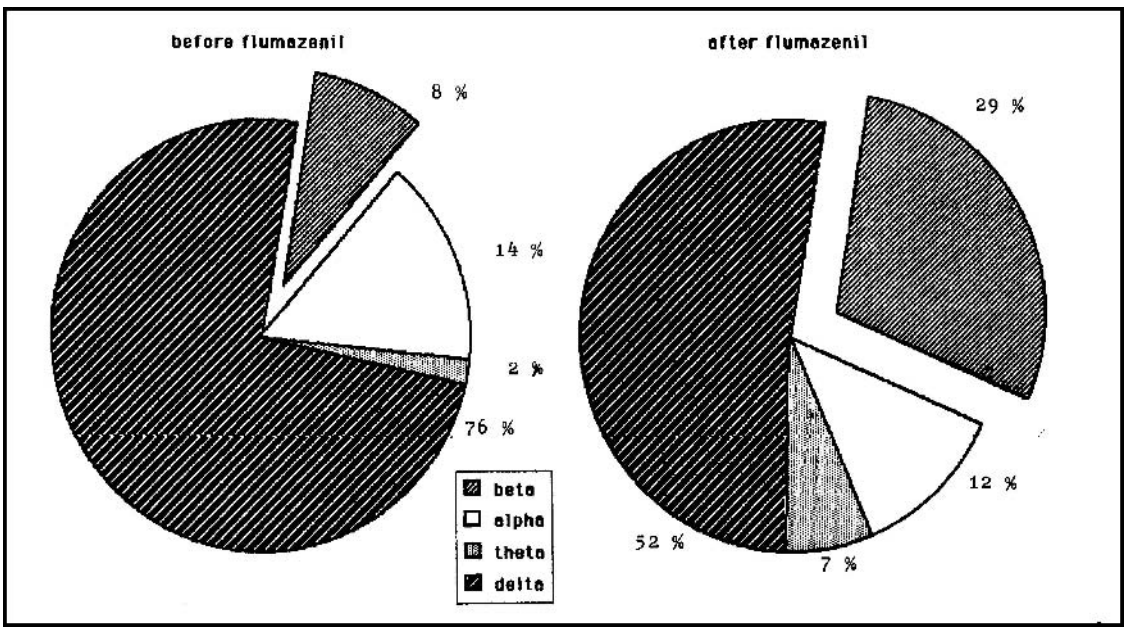


Fig. 67. Percent changes in EEG power spectra of patients in the ICU receiving benzodiazepines for sedation to tolerate ventilatory support (n = 10). In order to differentiate between primary brain lesion and drug overhang, the benzodiazepine antagonist flumazenil was given. The drug induced a marked increase in beta activity reflecting arousal. The time necessary for ventilatory support could be reduced.

received a total of 80 mg of diazepam over the past 24 h (Figure 68).

Neurologic exploration was difficult as the patient was in a deep comatose state. Computer tomography gave no clue in regard to intracerebral lesions, and since severe brain contusion was suspected, increments of the specific benzodiazepine antagonist "flumazenil" were given in repetitive doses of 0.2 mg. The pathological power in the delta band, as visualized in the on-line EEG power analysis, could not be reversed, and the compound could evoke no fast frequencies. Thus, the deep coma was due to cerebral lesion from which the patient never recovered.

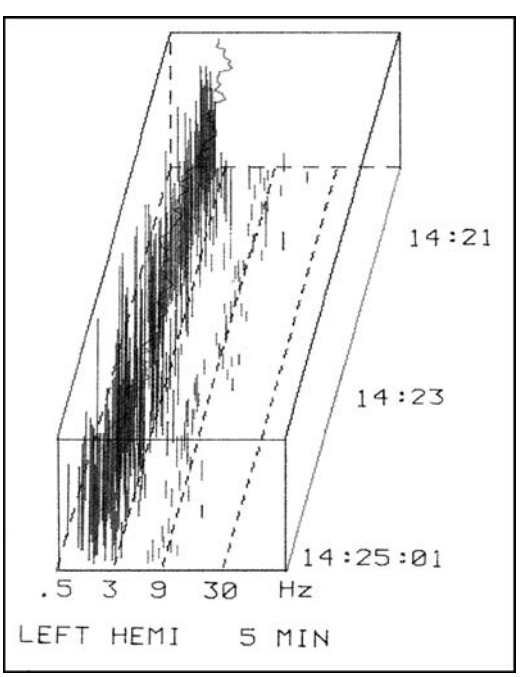


Fig. 68. Power spectra in a patient after severe head trauma. Although an overhang of diazepam was suspected, pathological slow waves could not be reversed by the specific antagonist flumazenil totaling up to 1.0 mg. Trauma related coma was diagnosed.

Cessation of cortical functions and brain stem trauma

A number of times monitoring of cortical activity is a prerequisite for diagnosing brain death. Apart from other symptoms (Table 5) the EEG ascertains the diagnosis displaying isoelectricity with no power spectra.

Under the supposition that no muscle relaxant, benzodiazepine and/or barbiturate overhang is present, all of which may mimic some of the above-mentioned symptoms, and that an existing electrolyte disturbance is corrected, the EEG (with its power spectra) is a necessary tool in determining cessation of brain function. The neurophysiologic

Table 5. Summary of symptoms suggestive for brain death

1. Unconsciousness
2. No reaction to nociceptive stimuli
3. Loss of muscle tone
4. Maximally widened pupils with no reaction to light
5. Fixed divergence of both eyes
6. Respiratory arrest
7. Hypothermia or poikilothermic reaction
8. Loss of circulatory regulation
9. Spinal reflexes
10. Loss of brain-stem reflexes (gag, occulo-cephalic, and occulo-vestibularis reflex)
11. Loss of pupillary and corneal reflex
12. Negative apnea test (an increase in CO_2 results in no respiratory movements)

evaluation thus comprises not only the effect of: (a) nociceptive, and (b) auditory stimuli on EEG activity. In some centers additionally, auditory evoked potentials (AEP) with special reference to the early peaks (=brain stern auditory evoked potentials = BAEP) are mandatory for the determination of brain death which may or may not be followed by angiography of the carotid arteries to establish absence of cerebral blood flow (indepth coverage on BAEP see chapter on "Acoustic Evoked Potentials").

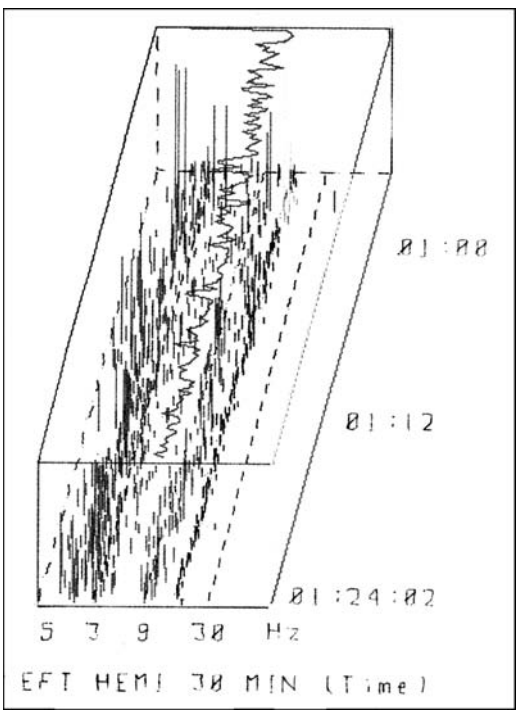


Fig. 69. Compressed spectral activity of a patient with coma vigil. Note power spectra besides depicting a pathological dominance in the slow delta range; also incorporate fast alpha activity, which may lead to misinterpretation of the patient's status.

Avoiding false interpretation of the compressed EEG signal

Aside from above representative examples, which underline the usefulness of compressed EEG analysis in the ICU, it is mandatory that during each period where power spectral analysis is performed that the raw EEG signal should always be inspected beforehand. Otherwise, undetected artifacts would go into the process of EEG analysis resulting in false information. One such "false information" was derived in a 65-year-old patient who had undergone prosthetic implantation of the brachiocephalic truncus and postoperatively acquired mediastinitis and hypotension with renal insufficiency. After a neurologist diagnosed extensive neurological examination intravital brain stem dysfunction, as there was a loss of brain stem related reflex activity. In the computerized EEG analysis, a dominance of delta and theta waves is evident, with interpolated alpha activity suggesting viable cortical action (Figure 69). It was only with the aid of the somatosensory evoked potential (see chapter on evoked potential monitoring) that a significant functional deficit could be diagnosed with a loss of the early peak, suggesting cortical and thalamic-cortical malfunction. As compressed cortical electrical activity only picks up potential changes from the outer cortical layers, a coma vigil was diagnosed. Thus, in critical situations it is necessary not only to rely solely on compressed EEG analysis, but also simultaneously take into consideration neurological tests and other neurophysiological data in examining CNS function such as the evoked potential.

Detection electrical interference with the EEG

The need to inspect the raw EEG signal in cases of doubt is demonstrated in another example, where compressed power spectra were derived in a patient after successful resuscitation (Figure 70). Aside from the pathological slow waves in the delta domain, regular "jig-saw"-like spectral edge activity results from changes in the fast alpha and beta activity. However, the missing power in the theta-domain raises suspicion for an interference with another electrical source. The search for the possible cause of such electrical interference may be troublesome as the intensive care unit is contaminated by various electrical currents and electrical machinery plugged to the socket, all of which act like small radiotransmitters. Inspection of the raw EEG wave visualizes that the incoming signals are 'contaminated' with a sinoid-like slow wave which, when crossing the zero-line, mistakenly was analyzed as delta activity. The cause of this

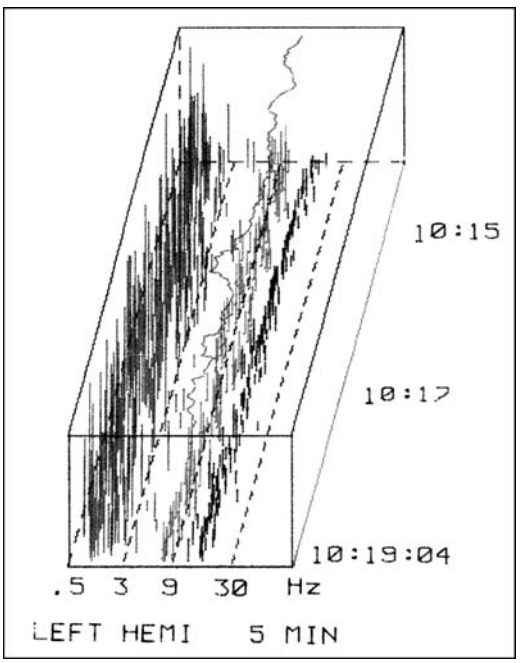


Fig. 70. Compressed spectral analysis in a patient with coma vigil. The dominant delta activity is an artifact induced by sweating. The missing theta activity (range 4–8 Hz) is suspicious for an electrical artifact being induced by poor electrode contact. The high electrode impedance could verify the latter.

"contamination" was perspiration of the patient, and once fresh ones replaced all electrodes, only fast activity was evident. In such instances a different type of electrode should be used, preferably needle or cup electrodes.

Thus, coma vigil was diagnosed, as neurological tests and the missing theta wave component further supported the suspicion.

As outlined above, cerebral monitoring in the intensive care as well as in the operation room may become a problem when interference from other electrical appliances is present. These interferences may evolve from:

(a) An infusion and/or a motor driven pump,
(b) A mechanical ventilator,
(c) A dialysis machine,
(d) A scan light,
(e) A screen for direct reading of blood pressure and central venous pressure, and
(f) An electrocardiogram.

Artifacts in the EEG arising from the patient

But aside from these electrical interferences, which are readily detectable as they are rhythmic in nature and induce a fluctuation of the base line, artifacts, which arise from the patient, also have to be taken into account.

An alcoholic with right sided brain' stem lesions (CT verified) who was being ventilated postoperatively after esophageal resection, showed beta activity in the EEG. It was suspected, that power in the beta range, which otherwise would only be found in awake and not sedated patient, was due to muscle tremor. A small dose of a competitive muscle relaxant underlined the suspicion, as shortly after the injection, power in the alpha and beta domains ceased completely, resulting in a dominance of pathological slow waves (Figure 71).

Paradoxical delta EEG waves

Paradoxical delta EEG waves, also termed as "paradoxical arousal" are occasionally seen in patients emerging from anesthesia or who intraoperatively during steady state anesthesia suddenly are exposed to a surgical stimulus [84]. It was first described in 1976 where a small percentage of patients during both anesthetic maintenance and emergence showed an unexpected slowing of EEG waves (high amplitudes with low frequency in the 0.3–4 Hz range), which usually are interpreted as signs of anesthetic deepening. Since slowing of the EEG resulted in an increase of EEG waves in the delta frequency band, it was also referred to an "arousal delta" because the expectation was that the patient was arousing from anesthesia while paradoxically generating delta instead of alpha or beta waves (Figure 72).

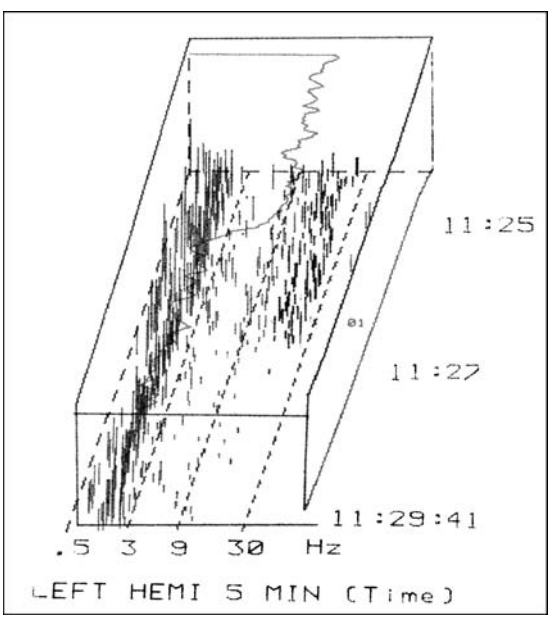


Fig. 71. Effect of tremor on EEG power spectra in a patient being sedated in the ICU. Injection of a muscle relaxant (event 01) ceases power in the alpha and beta domain.

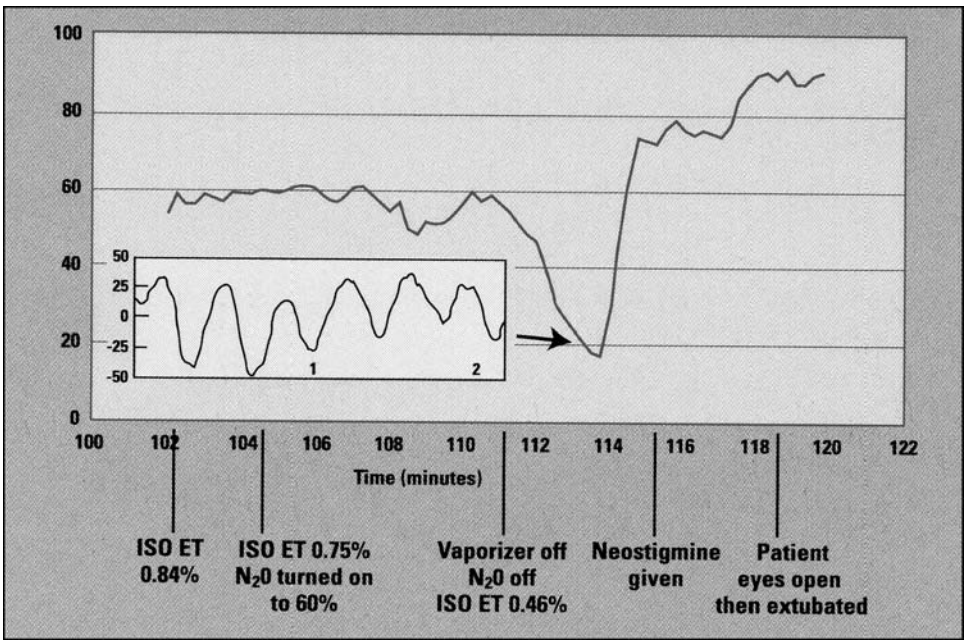


Fig. 72. Representative example in a patient, where in anticipation of surgery end isoflurane was dailed down at the vaporizer. The derived BIS value demonstrates a dramatical decline due to the appearance of paradoxical EEG slowoing.

While ist was speculated that paradoxical arousal may happen from surgical response [85, 86], where nociceptive affrents arise from deeper tissue structures, or in response to anesthetic lightening [87], it apparently is 10 times more likely to occur during inhalational anesthesia as opposed to parenteral anesthetic agents. While it it generally agreed upon that other physiological pathologies can increase delta activity, one should consider the event always in the clinical contect. What type of procedure is being done, what events relate to surgery or anesthesia, evaluation of the patients vitals signs, icluding oxygen sarturation, end-tidal CO_2, with particulat attention to the possibility of hypoxia, hypotension or hypothermia. The paradoxical arousal by itself is a short lived event lasting for several minutes. If the condition persit for longer than 10 min, re-eravaluation of all clinical paraneters for potential causes is mandatory.

EEG power spectra during normal sleep

Apart from the use of continuous, compressed and computerized electroencephalographic analysis in the operation room, the intensive care, as well as the emergency and the detoxification units, also sleep researchers find this technique a useful adjunct for overnight monitoring in cases of insomnia. Due to a storage capacity of up to 10 h and longer, the capability to store overnight EEG recording on disk makes this technique an attractive alternative to the usual strip chart recording (Figure 73).

A representative example of overnight sleep recording of the author shows the compressed and processed EEG data over a time axis of 5 min at 2.00 a.m. depicting different stages of sleep. At 2.09 a.m. fast frequency in the beta range becomes visible suggesting start of REM stage (rapid eye movement), a pattern that is accompanied by artifacts from eye movements. Shortly thereafter, and concomitantly with the appearance of fast activity, power in the slow delta domain drops suggesting REM sleep which according to sleep researchers, primarily is associated with dream activity. This kind of processed recording has not been fully evaluated to its full potential in sleep research. Whether the compressed analysis in comparison to strip chart recording contains more information for the physician dealing with sleep disorders remains to be proven (Figure 74).

Trouble shooting when monitoring the brain

This section is intended to aid the user of computerized EEG analysis in solving minor operational and technical problems, which might arise in the course of processed EEG monitoring (Table 6). Since in the majority of cases problems in recording are due to electrode misconnection and/or electrical interference, defaults, which arise from

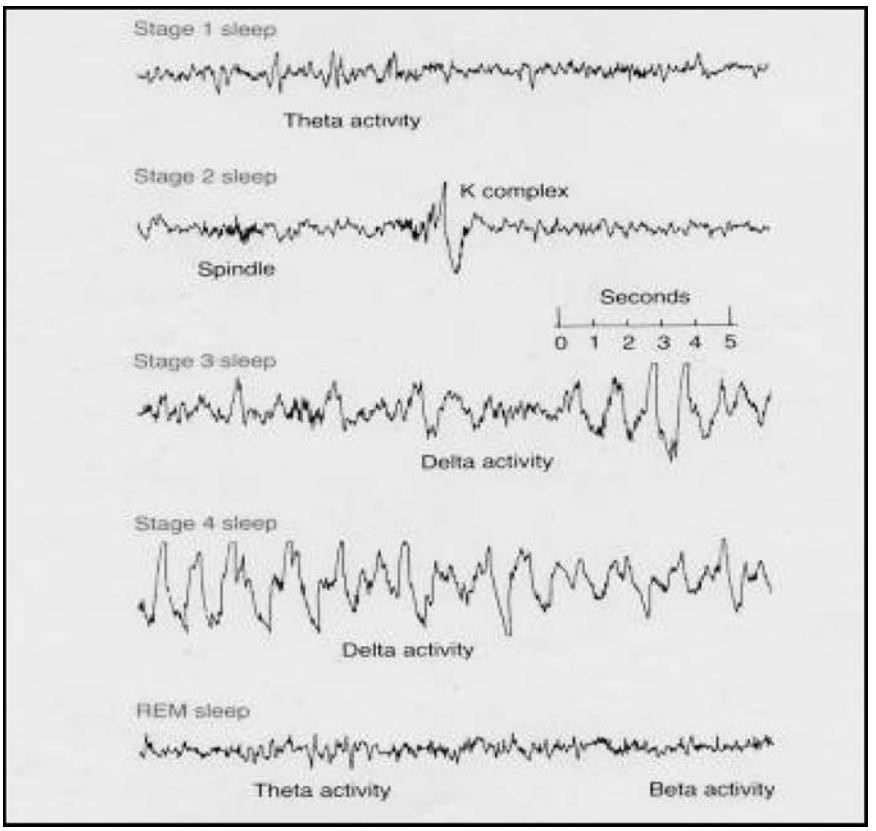


Fig. 73. Characteristic pattern during sleep recording with different sleep stages. From slow wave sleep with high activity in the delta band there is a change to REM sleep. The latter is associated with activity in the fast domain and a reduction of power in the delta band.

the central processor of the internal circuit of the EEG device, will not be dealt with:

1. The major problem in all EEG recordings are artifacts, which arise from the recording electrodes themselves. As mentioned above for any EEG channel that indicates impedance above 5 kΩ the electrode on the skin has to be checked and possibly replaced. Before doing so, the skin has to be cleaned thoroughly with alcohol from electroconductive gel and one has to make sure that the site of application is completely dry.
2. If, during the recording procedure, a gradual increase in impedance is noted, this can be considered as a warning signal for an improperly functioning adhesive disc electrode, which tends to come off. One can solve the problem by simply replacing the pregelled conductive electrode unit after thorough cleaning and drying the site of application.
3. Often there are cases where due to intense sweating of the patient any disc electrode will tend to come off (Figure A3). The EEG signal then is characterized by

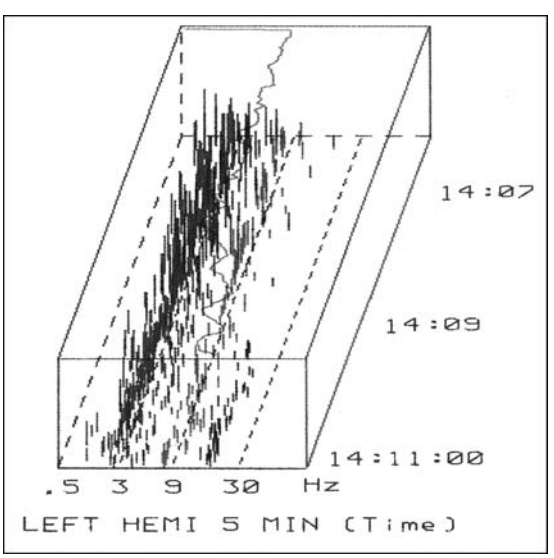


Fig. 74. EEG compressed spectral analysis during overnight sleep recording. Change from power in slow delta- to theta-band (slow wave sleep) to dominance in the fast beta band. The latter is indicative for REM sleep.

Table 6. Summary of possible artifacts during EEG recording

A. Biological artifacts
1. Eye lid movement
2. Muscle activity during swallowing
3. Sweating, movements of arms and legs
4. ECG cables running across EEG leads thus picking up myocardial activity from the heart
5. Muscle tremor
B. Interference from surrounding electrical appliances
1. AC current interference due to improper grounding
C. External interference from people in the room
1. Movements in the room where EEG is taken
2. People pacing in the room where EEG is taken
3. Plexiglas is being moved on table near the preamplifier
D. Electrodes and connections
1. Artifact due to cable movement
2. Improperly fixed reference electrode during bipolar recording
3. High impedance $>5\,K\Omega$
4. Faulty insulation of electrode

large fluctuations of the base line, which is processed as EEG activity in the delta range. This is the one exception when in EEG recording subdermal needle electrodes are advocated. Also, cup electrodes fastened to the skin by a glue-like material (collodion) do a similar job.

4. High static waves in the raw EEG signal are one example where an interference with other electrical appliances is the likely cause. In such cases one should try to ground all other electrical units nearby as the electrical noise in the EEG is due to AC current flowing freely through the room (Figure B1–2).
5. Also, an uncooperative patient, or a patient who is in a hyperactive state will result in artifacts arising during the recording period. Such situation also is characterized by an excessive base line wandering (Figure AI,2,4). In such instances the patient has to be sedated.
6. External interference from the body of the physician touching the patient and/or people walking by often tend to result in static charges (Figure CI–2), which are picked up by the sensitive EEG preamplifier and reflected in the processed EEG. One easily can to solve such problem by stopping everyone from moving about. Similar static discharges can be induced by movements of plexiglas near the preamplifier (Fig, C3).
7. Any electrode cable disconnection and breakage tends to induce fluctuations, which are either identified as artifacts or processed as slow waves in the delta range. Thus, if there is any doubt about the results as they are processed from the raw EEG, one should check the raw EEG waves, which are fed into the computer. Such a procedure usually is very simple by activating a touch key indicating "raw EEG signal", thus identifying the cause of malfunction (Figure DI–4).
8. Excessive artifacts in the raw EEG signal may be due to a number of reasons:

   (a) Accidentally jarred leads of the preamplifier,
   (b) Gross muscle movements,
   (c) Electrocautery,
   (d) 50–60 Hz power line interference,
   (e) Electrodes not properly prepped or gelled, and
   (f) Faulty electrode leads.

   Prior to all processing, such problems can be eliminated by making certain that electrodes are prepped, that electrode leads do not run across a power line, and by replacing all faulty electrodes. 50–60 Hz electrical noise can easily be identified on the raw EEG signal. One has to localize the source and switch off the nearby electrical machine. Electrocautery will result in no proper recording with any device. In such a case, the electrodes pick up the electrical current running inside the organism and the signal fed into the preamplifier. For optimal recording one has to wait till electrocautery is finished. In addition it should be borne in mind that improper grounding of the electrocautery unit may result in local skin irritation with burn marks at the site of EEG electrodes. However, sufficient electrode gel between the electrode disc and the skin will prevent this from happening.
9. Seldom, although the unit is turned on, no EEG signal is displayed on the EEG monitoring screen. Then a check of proper connections of all electrode cables to the preamplifier and the preamplifier socket connection to the main unit has to be undertaken. In rare cases a faulty preamplifier or a disrupted lead are the cause of such a problem (Figure 75).

SYSTEMS CURRENTLY AVAILABLE FOR PROCESSED EEG RECORDING

The bispectral index (BIS) – monitoring the level of consciousness during anesthesia and sedation

Bispectral analysis is an advanced signal processing technique that is capable of tracking non-linear as well as linear changes in signals. An analysis technique, which can detect and quantify non-linear changes, better reflects the

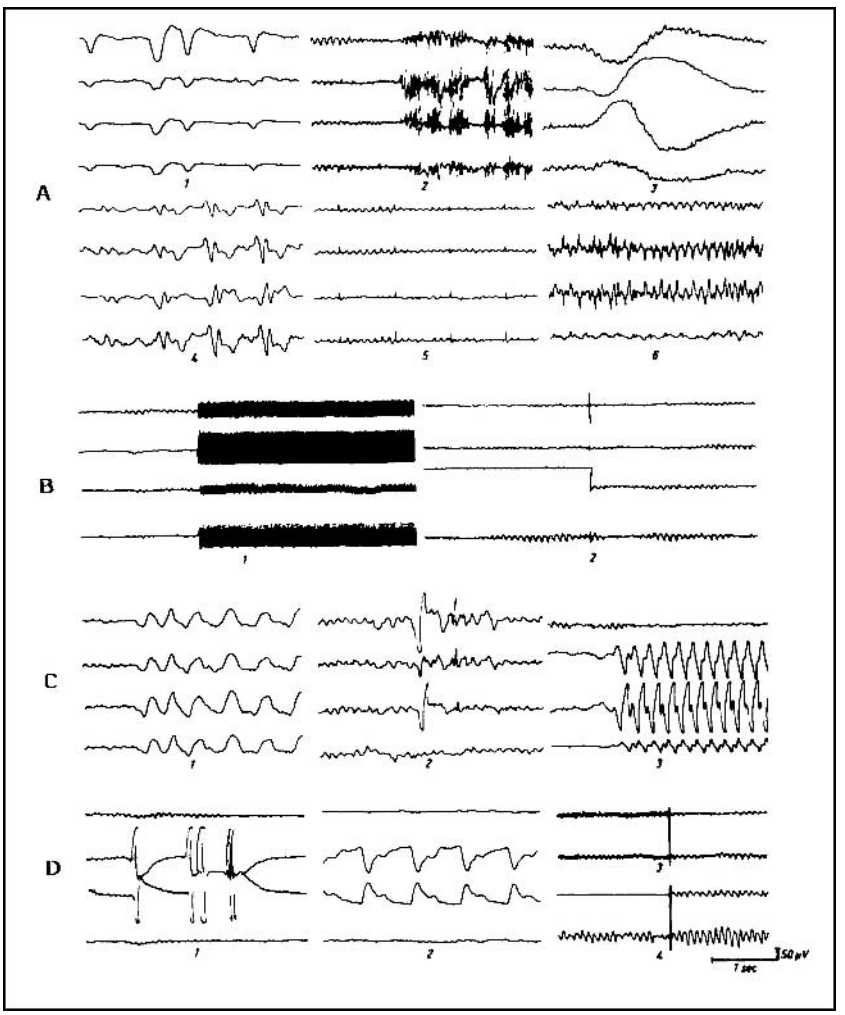


Fig. 75. Summary of possible artifacts interfering with the native EEG wave resulting in electrical interference from in- and outside the patient.

dynamic structure of the EEG than one that cannot. Therefore, the bispectrum is claimed to be a more suitable analysis tool for quantifying subtle changes in brain electrical activity.

Geophysicists first used Bispectral analysis in the early 1960's to study ocean wave motion atmospheric pressure changes, seismic activity, and sunspots. Early on, it was also used to study the EEG's interfrequency coupling in a number of states including waking and sleep. Because of the heavy computational requirements of bispectral analysis, little work was generated for over a decade, except for military applications. More recently, with the advent of high speed, low cost computing, new research is emerging on processing biological signals, including the EEG and ECG, utilizing bispectral analysis. Such research included the assessment of anesthetic adequacy [88–91], the reduction of awareness during anesthesia [92–94], the depth of sedation in the ICU [95–97], and the evaluation of the induction dose in the OR under clinical conditions [98, 99]. These studies have indicated that useful information may be extracted from the EEG using bispectral analysis, beyond that which is available in the power spectrum.

The mathematical approach of bispectral analysis relies on the expansion of the widely used Fourier Transform method of signal decomposition into simpler component waves. Conventional power spectral analysis assumes that all component sine waves of a signal are independent (fundamentals), whereas bispectral analysis measures the potential interrelations between the waves to determine whether dependent (harmonic) components are present. For example, if two fundamental waves are generating a harmonic, the

harmony's frequency is equal to the sum of the frequencies of these fundamentals and the phase of the harmonic is equal to the sum of the phases of its fundamentals. Using this principle, bispectral analysis quantifies the degree of phase coupling between every possible frequency pair combination and the frequency at their sum in order to determine if the component waves are harmonies or fundamentals. Averaging over time the difference between the sum of the phases of the two fundamentals, and the phase of the third component at their frequency sum does this. If the difference is "0", then the third frequency wave is a harmonic of the first two. At any one frequency, there may be independent fundamental contributors as well as harmonic contributors. Bicoherence represents the degree of phase coupling or harmonies present at each frequency and is a continuous variable that ranges between 0 and 100%. A linear system will produce a signal with 0% bicoherence, whereas non-linear systems typically exhibit some degree of bicoherence (Figure 76).

In addition to the information regarding the overall degree of phase coupling (bicoherence) throughout the signal, bispectral analysis can also provide information regarding the absolute and phase-locked power content at each frequency location. Calculation of these complex data "arrays" is a computationally intensive process, which results in a more comprehensive description of the EEG signal and thus is claimed to be able to detect more subtle changes than conventional techniques (Figure 77).

The task of extracting clinically useful information from the bispectrum is one of determining how changes in the bispectrum relate to changes in the EEG during periods of altered cerebral function, such as the administration of anesthetics and neuroactive drugs, ischemia, and hypothermia. Visually, certain general patterns in the raw EEG signal have been recognized during anesthesia when anesthetic doses are increased. It has been noted that the EEG signal slows down and appears to become more synchronized. Power spectral analysis provides some identification of the "slowing down" via increased delta frequency content. Bispectral analysis trends these changes as well, but also provides a measure of synchronization via the degree of phase coupling. Bispectral analysis is still subject of active research, and several investigators have demonstrated that it provides useful information concerning the patient's cerebral state during the administration of anesthesia [100–102]. Aspect Medical Systems has reduced the complex data arrays generated from bispectral analysis using a sophisticated algorithm to generate a composite, numerical Bispectral Index which tracks changes in the cerebral state. This Bispectral Index quantifies the overall bispectral properties (frequency, power and phase) throughout the entire frequency range in a simpler format than the basic three dimensional bispectral arrays (Figure 78).

The BIS index is a combination of four components within the EEG. Because it takes into account:

a. The low frequency feature, as it is seen in deep anesthesia,
b. A high frequency feature, which is associated with a light anesthetic plane, and beta- activation, it also incorporates
c. The degree of suppressed EEG waves, and
d. The degree of burst suppression

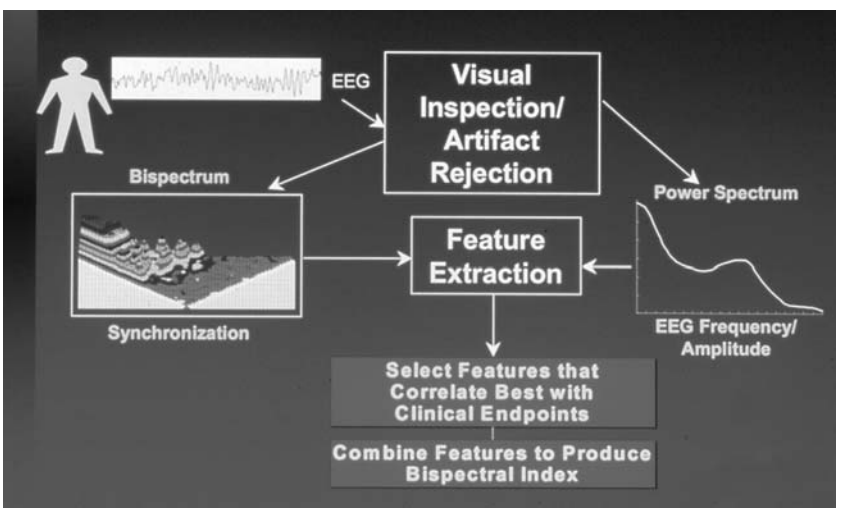


Fig. 76. Graphic view of the basics in evaluating the bispectral index (BIS) from the raw EEG signal taking into account the interrelation and phase-coupling between waves.

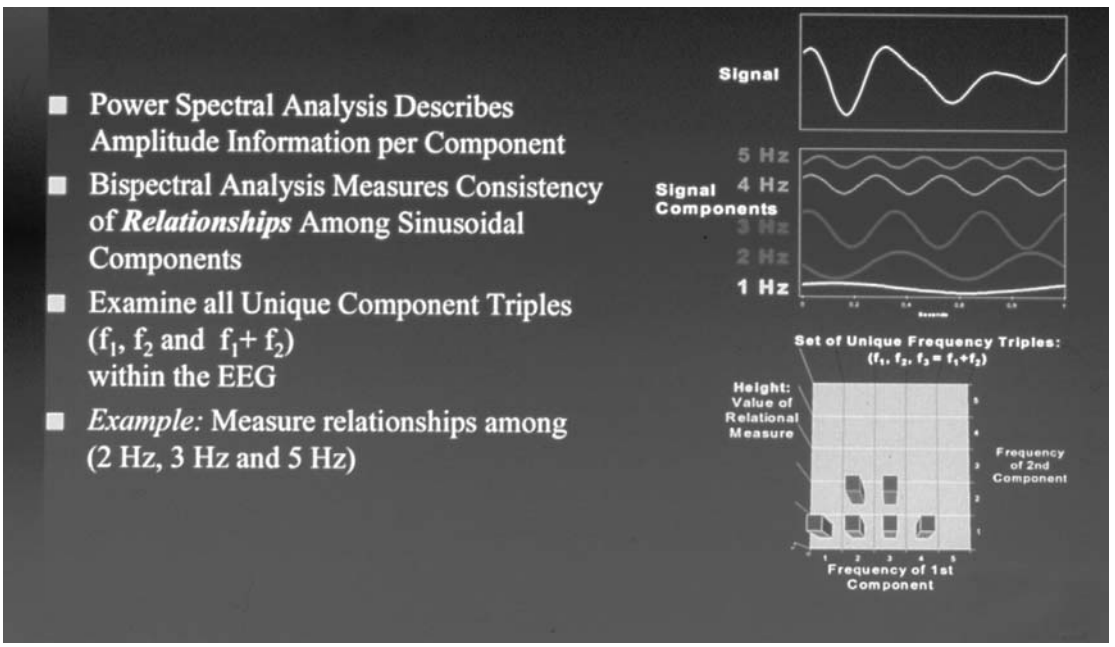


Fig. 77. Basic steps in BIS algorithm determining the inter-component relationship.

Since the BIS quantifies the relationship between various EEG frequency bands (who are in phase) and computes the correlation by coherence coupling (the degree of phase coupling) it is tooted to predict the responsiveness to noxious stimuli, demonstrating a higher sensitivity to anesthesia-related changes than the routine Fast Fourier Transform, which is used in most other computerized EEG-devices. When used in the context with other variables usually taken during anesthesia, it gives further insight as to the cause of the underlying changes (Figure 79).

Numerous studies have demonstrated that the BIS is able to reduce the incidence of awareness, especially during CABG surgery, a reduction in the dose of the hypnotic necessary to render the patient unconscious, a faster recovery rate with earlier extubation times, a shorter stay in the PACU, and a marked reduction in costs of anesthetics being used. In addition, a specials set of sensors has been developed, where the three pre-gelled electrodes are integrated within a band set which is applied to the front head thereby reducing the time necessary for electrode set-up (Figure 80).

All BIS data so far empirically have been correlated with different stages of anesthesia in over 900.000 cases suggesting a sufficient overall close association between the BIS value and the level of anesthesia. However, it should be borne in mind that during the induction with propofol, high dose opioids and with the use of ketamine, the BIS tends to give false values in regard to patients level of unconsciousness. Also, the BIS is not an indicator of sufficient analgesia as it measures only the hypnotic effect of an anesthetic. If, however, a nociceptive impulse results in an increase in the level of vigilance the BIS will go up, indicating a lighter plane of anesthesia.

A close correlation of the BIS value with brain metabolic activity was demonstrated in a study with PET scan using the metabolic rate of glucose (Figure 81).

Entropy, an algorithm for the native EEG taking into account the activity of the frontal muscle

Entropy is an innovative monitoring modality, which is designed to provide information on the state of the central nervous system during general anesthesia. Entropy monitoring is based on acquisition and processing of raw EEG and facial EMG signals by using the Entropy algorithm, originally developed by Datex-Ohmeda (Finland). Spectral entropy is now being marketed by GE Healthcare Technologies (Entropy S/5′M Monitoring system), which can be used as an aid in monitoring the wakefulness during anesthesia [104–107].

Although the primary target of anesthetic drugs is the CNS, most anesthesiologists confine monitoring during anesthesia to cardiocirculatory and respiratory parameters. Among other reasons, this is because the measurable signals

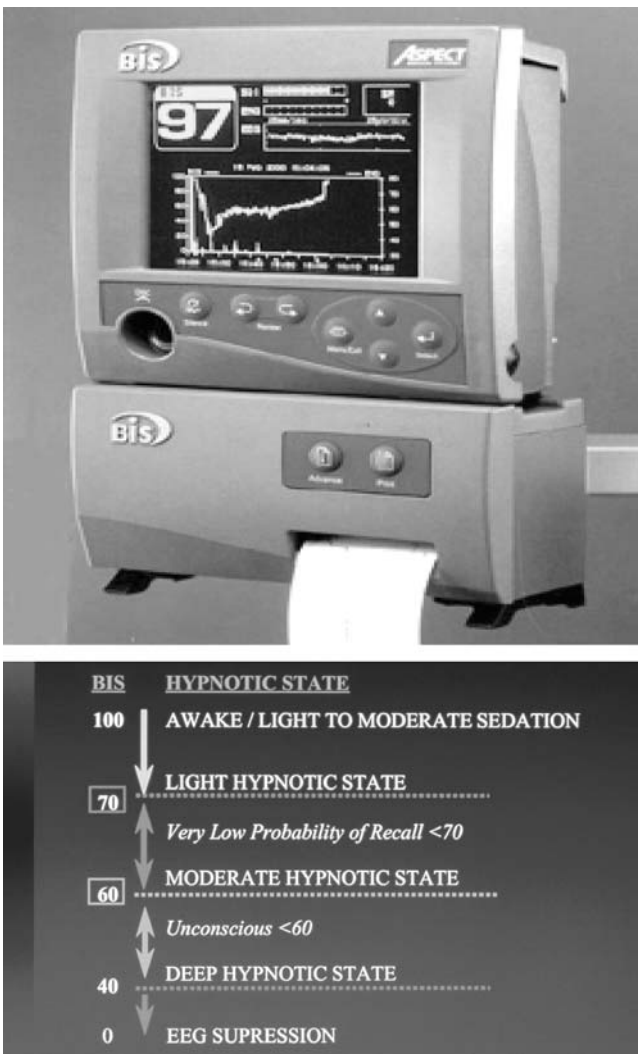


Fig. 78. The Aspect EEG monitor depicting the BIS value during anesthesia which is able to reflect different hypnotic states.

coming from the CNS such as the electroencephalogram (EEG) or evoked potentials are difficult to interpret. Researchers therefore have attempted to condense the complex information of the EEG into a single parameter. Examples of such parameters tested over many years are the spectral edge frequency or the median frequency of the power spectrum of the EEG [108, 109]. However, these parameters have never entered widespread clinical practice for two reasons: they are sensitive to artifact, and they are also difficult to interpret due to the biphasic concentration-response relations with some drugs. Further developments have resulted in parameters derived as a weighted combination of several sub-parameters. The most familiar of these is the Bispectral Index (BIS), now widely accepted and supported by many experimental and clinical studies [110].

New mathematical developments and advances in computer technology have now made several different approaches available to EEG analysis, especially those derived from information theory. Several new parameters derived from the EEG have been suggested such as approximate entropy, correlation dimension, and spectral entropy [111–113].

Spectral entropy of the EEG has become commercially available in the Datex-Ohmeda S/5 Anesthesia Monitor using the M-Entropy module and after a merger, is now being marketed by General Electric. In addition to a new computational approach of EEG analysis, this monitor also takes into account new developments in the concept of "adequacy of anesthesia". Contrary to previous assumptions, the anesthetic state is now understood to consist of several components, including unconsciousness, amnesia, antinociception, immobility and autonomic stability. Since only unconsciousness and amnesia are considered to be of cortical origin, parameters of the EEG are likely to correlate only with these cortical components of anesthesia. In contrast, spontaneous muscle activity measured as the frontal electromyogram (FEMG) is influenced by subcortical structures. The M-Entropy module, using a single sensor, gives two separate readings: one for the spectral entropy of the pure EEG signal (state entropy) and the other for the spectral entropy of the combined EEG-FEMG signal (response entropy).

In a clinical evaluation trial, entropy was tested with the new M-Entropy module during routine anesthesia cases in the urological and gynecological OR suites of the Charité University hospital in Berlin. As a training hospital, staff varies from first year trainees to senior anesthesiologists. A wide range of procedures is performed, from short diagnostic ones to renal tumor resections under cardiac bypass.

The overall response of the participating anesthesiologists was positive. Entropy values generally correlated well with the clinical evaluation of anesthetic adequacy by the anesthesiologist in charge. This correlation seemed to be better for experienced anesthesiologists. Conversely, especially colleagues in training thought that the additional monitoring information was helpful to countercheck their clinical assessment. Nevertheless, even experienced anesthesiologists admitted that the entropy readings were reassuring in cases where interpretation of anesthetic adequacy was difficult. Specifically, cases where cardiocirculatory parameters were largely influenced by factors other than anesthetic depth (e.g. adrenalectomy), and patients whose anesthetic requirements were difficult to assess (e.g. morbidly obese patients).

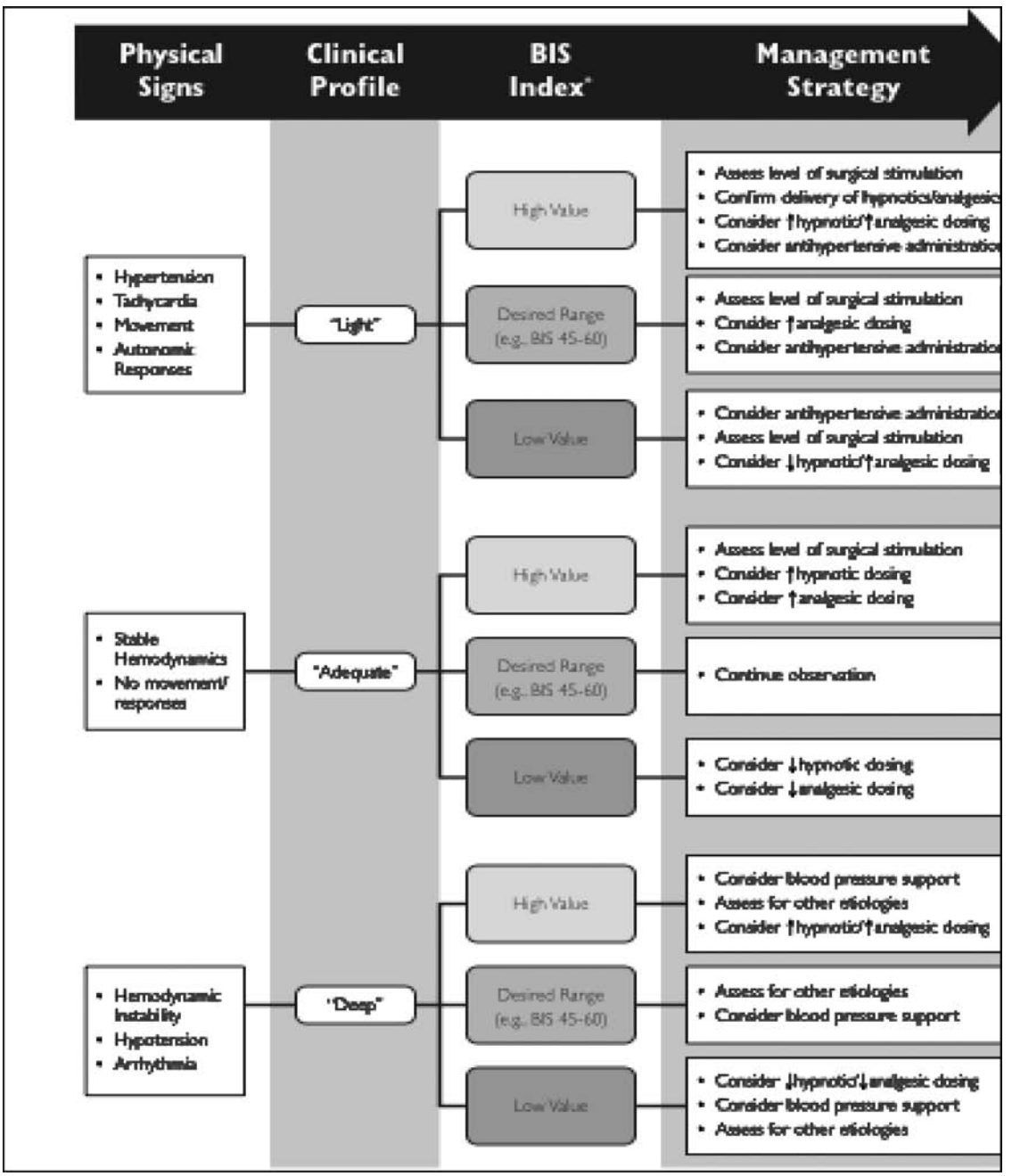


Fig. 79. Algorithm in anesthesia management strategies using the BIS index.

Evaluation of the signal stability revealed low variability of the baseline signal, estimated as less than 5 % (median baseline value for state entropy = 88.5). Eye movements, which have been a problem with some previous devices, did not appear to alter the entropy measurement. During surgery, the entropy signal was stable even during electrocautery, which traditionally has been a problem with neuromonitoring. During anesthesia considered as adequate for surgery by the anesthesiologist, entropy values were in the range of 40–60, and appeared to be stable at constant levels of surgical stimulus and anesthetic concentration.

Since there is no "gold standard" of anesthetic depth with which to compare the entropy values, the evaluation is inevitably subjective. There were times where clinical

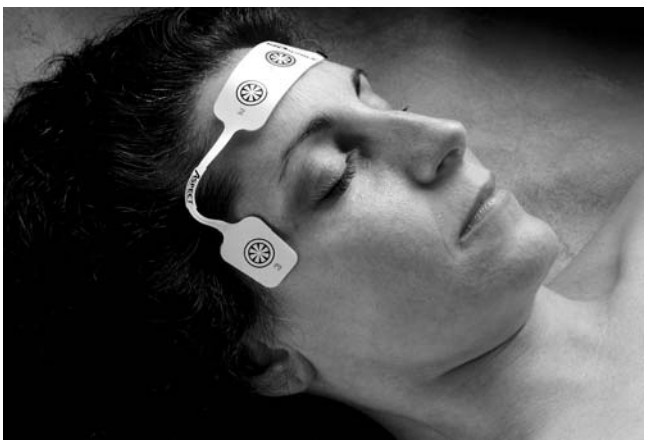


Fig. 80. The BIS-electrode, a set of three sensors integrated into a band set, which rapidly can be applied to the patient's fronto-temporal side of the head for immediate measurement.

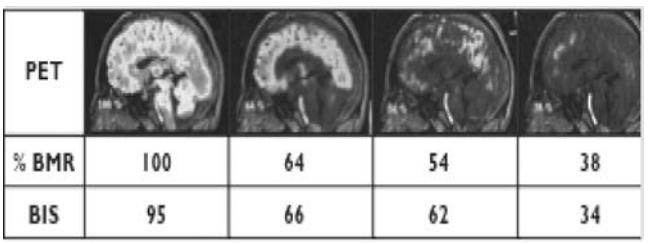


Fig. 81. Brain metabolic rate (BMR in % from the initial whole brain glucose metabolism measured from PET) and the simultaneous reduction in BIS with increasing concentrations of a volatile anesthetic. Adapted from [103].

judgment and entropy differed even among experienced anesthesiologists. We cannot say whether anesthesia was truly adequate or inadequate at that time; that question must be addressed in outcome-oriented studies.

Since the monitor differentiates between "state entropy", stemming from cortical EEG signals, and "response entropy", including EMG activity, it became clear from this evaluation that monitoring the effects of anesthetics on the central nervous system is a welcome addition to the armory of the practicing anesthesiologist. This requires monitoring devices, which are easy to use and easy to interpret as well being resistant to artifacts. The entropy monitor appears to be promising on all these points. In addition, it is difficult to prove that entropy monitoring prevents unwanted outcome. It however, can be assumed that it helps as an "aid to vigilance", offering reassurance especially in difficult situations.

By adding the measurement of the cortical electrical activity the clinician can assess the effect of anesthetics more comprehensively. Electroencephalography (EEG) changes from irregular to more regular patterns when anesthesia deepens. Similarly, frontalis electromyography (FEMG) quiets down as the deeper parts of the brain are increasingly saturated with anesthetics. Entropy measures the irregularity of EEG and FEMG signals. The special Entropy sensor is attached on the patient's forehead (Figure 82). The sensor features the familiar peel-place - press functionality and forms a good contact with skin. The Entropy sensor cable connects the sensor to the Entropy module and no headbox is required.

Monitoring electrical activity of the brain and facial muscles with the Entropy Module is intuitive. One attaches the Entropy sensor on the patient's forehead according to the instructions provided on the sensor pouch. The module automatically checks that the electrode impedances are within an acceptable range and starts the measurement. The measurement will continue until the sensor is removed.

Entropy numbers have been shown to correlate to the patient's anesthetic state. High values of Entropy indicate high irregularity of the signal signifying that the patient is awake. A more regular signal produces low Entropy values, which can be associated with low probability of consciousness. There are two Entropy parameters: the fast-reacting Response Entropy and the more steady and robust State Entropy. State Entropy consists of the entropy of the EEG signal calculated up to 32 Hz. Response Entropy includes additional high frequencies up to 47 Hz. Consequently the fast frontalis EMG (FEMG) signals enable a fast response time for RE (Table 7).

The Entropy module provides a quantitative measurement by producing two parameters describing the effects

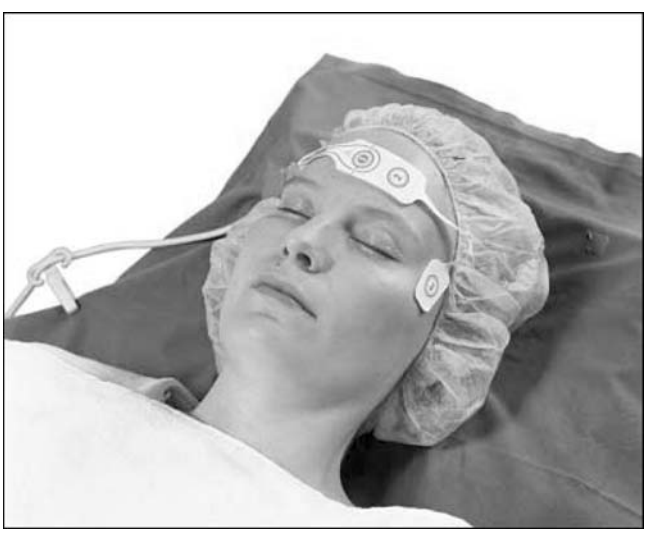


Fig. 82. Placement of the entropy sensor on the forehead of the patient.

Table 7. Frequency and display ranges for entropy parameters

Parameter	Measurement frequency rate	Display range
Response Entropy, RE	$0 < f < 47$ Hz	0–100
State Entropy, SE	$0 < f < 32$ Hz	0–91

Table 8. Entropy range guidelines as they are shown on the waveform field

100	Fully awake and responsive
60	Clinically meaningful anesthesia
40	Low probability of consciousness
0	Suppression of cortical electrical activity

of anesthetics on the patient's CNS during anesthesia (Figure 83).

a. Response Entropy (RE), which is sensitive to the activation of facial muscles (i.e. FEMG). Its response time is very fast, less than two seconds. FEMG is especially active during the awake state but may also be activated during surgery. Activation of Response Entropy to painful stimuli may be interpreted as a sign of inadequate analgesia. Facial muscles may also give an early indication of recovery, and this can be seen as a quick rise in RE.
b. State Entropy State Entropy (SE) value is always less than or equal to Response Entropy. Estimation of the hypnotic effect of anesthetic drugs in the brain during general anesthesia may be based on the State Entropy number. State Entropy is not affected by sudden reactions of the facial muscles because it is based on the EEG signal. Neuromuscular blocking agents (NMBA), administered in surgically appropriate doses are not known to affect the EEG. It is postulated that while SE is a index of the hypnotic state of the patient the RE may be used as an indicator of insufficient analgesia as nociceptive impulses, not sufficiently blocked by an analgesic agent, are transmitted via the brain stem where the facial nerves originates giving rise to an increased activity to the frontal muscle.

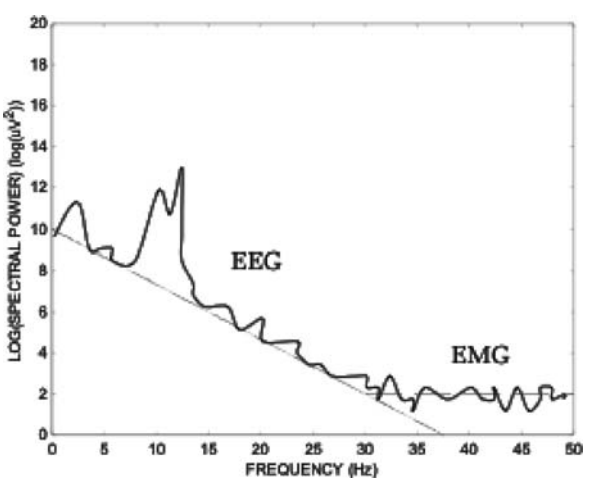


Fig. 83. Typical power spectrum of a biopotential signal measured from the forehead of a patient. The EEG signal dominates up to frequencies of about 30 Hz, while the EMG signal dominates a higher frequency range (vertical scale logarithmic).

Individual patients may show different values. Frequent eye movements, coughing and patient movement cause artifacts and may interfere with the measurement. Epileptic seizures may also cause interference. Entropy readings may be inconsistent when monitoring patients with neurological disorders, trauma or their sequelae. Psychoactive medication may cause inconsistent Entropy readings. Entropy module so far has not been validated with pediatric patients (Table 8).

Adequate anesthesia results from a balance of various components. Therefore, adequate anesthesia needs to be assessed with more than only one parameter. Entropy is apart of the bigger picture, as illustrated in Datex-Ohmeda's adequacy of anesthesia concept. When Entropy is used together with other monitored parameters, such as the hemodynamic and neuromuscular measurement, one can get a complete picture of the patient status combined on one screen.

The Patient State Index (PSI) to measure depth of consciousness

Being part of the Patient State-Analyzer (PSA4000®; Physiometrix/USA), the PSI presents another processed EEG parameter, which enables the clinician to assess brain state changes in response to drug dose titration and confirming adequate sedation and/or hypnosis to measure of depth of unconsciousness [114–116].

The Physiometrix 4000 PSA monitor is indicated for use in the operating room (OR), the intensive care unit (ICU), and the clinical research laboratory. It is intended to monitor the state of the brain by real-time data acquisition and processing of EEG signals.

The Patient State Index (PSI™) algorithm was constructed by using stepwise discriminant analysis based upon multivariate combinations of QEEG variables found to be sensitive to changes in the level of anesthesia but insensitive to the specific substances producing such changes. The

PSI is the result of a complex computation that combines weighted quantitative values reflecting many dimensions of brain electrical activity such as:

1. Changes in power in various EEG frequency bands;
2. Changes in symmetry and synchronization between critical brain regions and
3. The inhibition of regions of the frontal cortex.

The PSI^{TM} is computed from continuously monitored changes in the QEEG, during surgery, using statistical analysis to estimate the likelihood that the patient is anesthetized. The PSA 4000 performs these computations automatically on the continuously recorded EEG, after automatic deletion of artifacts interfering with data by physiological and environmental signals. Also, the computed PSI^{TM} is periodically updated, displayed in numeric form and presented in a color-coded trend graphic for monitoring the effect of certain anesthetics on the state of the brain (Figure 84).

Three databases were fundamental to the development of the algorithm: EEG Library (Database I), Surgical Cases (Database II), and Volunteer Calibration Study (Database III).

Database I was the electrophysiological database previously established in the Brain Research Laboratories (BRL) of New York University School of Medicine. This database contained approximately 20,000 raw and quantitative EEGs recorded from normal, psychiatric, neurological and surgically monitored patients. Statistical descriptors have been computed for the age-dependent normative distributions of numerous quantitative measures (QEEG) extracted from these recordings. These normative values have been shown to have high reliability, specificity, sensitivity, and significantly high test-retest replicability, as well as to show no ethnic or cultural bias. The BRL database also provided a library of the characteristics of artifact, non-EEG signals that were used to develop algorithms for automatic identification and real-time exclusion of artifact from subsequent data processing.

Database II was derived from continuous EEG recordings made in a large population of patients undergoing general anesthesia with a variety of agents, administered under standard clinical practice. Each procedure was carefully documented for anesthetic, hemodynamic and surgical events. In each case, quantitative EEG features were extracted under defined states and conditions. These features (approximately 2500 per session) included spectral and bispectral measures of power and coherence and were used to form a new database documented for state of consciousness. Systematic exploration of this database was used to identify a subset of features that changed in an invariant way with deepening levels of sedation-hypnosis and loss of consciousness and reversed with return of consciousness.

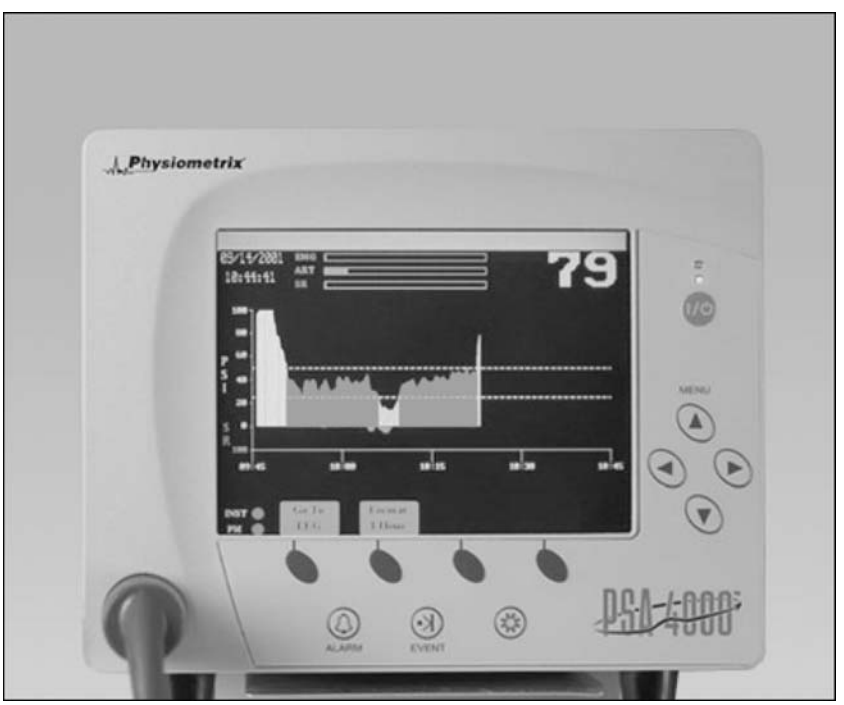


Fig. 84. Front view of the PSA 4000 EEG monitor with the integrated patient state index (PSI) in a numeric form.

Candidate measures were further explored using multivariate analysis to form mathematical classifier functions estimating the most probable level of consciousness. Candidate classifier functions were evaluated retrospectively for correlates of depth of sedation-hypnosis, as defined by the attending anesthesiologist. Details of the construction of this database and the retrospective analysis are given elsewhere.

Database III was derived from EEG recordings made during 64 procedures in which various anesthetics were administered incrementally (0.1 MAC steps to loss of consciousness and return of consciousness) to healthy volunteer subjects. QEEG and clinical measures extracted from this database were used to assist in the calibration of the PSI.

Algorithm processing in the computation of the PSI

EEG is collected from two anterior (FP1 and Fpz1), a midline central (Cz) and a midline posterior (Pz) scalp location, referenced to linked ears, utilizing circuitry optimized to exclude electrical contamination from the environment (Figure 85).

Using pre-gelled disposable Ag/AgCl electrodes printed on polyester substrate, active electrodes are positioned at Fp1, Fp2, Cz, and Pz. The ground is Fp2 and references are linked ears. This array was chosen because previous studies have demonstrated differences in electrical activity between different regions of the brain in patients undergoing anesthesia.

The signals are sampled at 2,500 samples per second per channel, band pass filtered to 0.5 to 70 Hz and then decimated to 250 samples per second per channel, in accordance with the Nyquist theorem.

EEG signals are then processed by a series of artifact detection algorithms, allowing the identification of artifact-free 'epochs' of EEG data. An additional algorithm detects EEG suppression, excludes these data from further algorithmic processing, and is used to compute a suppression ratio. This ratio can be monitored via the instrument's user interface and is taken into account by the PSI algorithm.

EEG data in 1.25-s epochs is frequency transformed into sub-bands (Figure 86), including delta, theta, alpha, beta, gamma and total power (0.5–50 Hz).

The set of features found to account for most statistical variance related to hypnotic state (selected from studies reviewed above) were derived for input to the discriminant algorithm (proprietary). These features included measures such as:

a. Absolute power gradient between frontopolar and vertex regions in gamma.

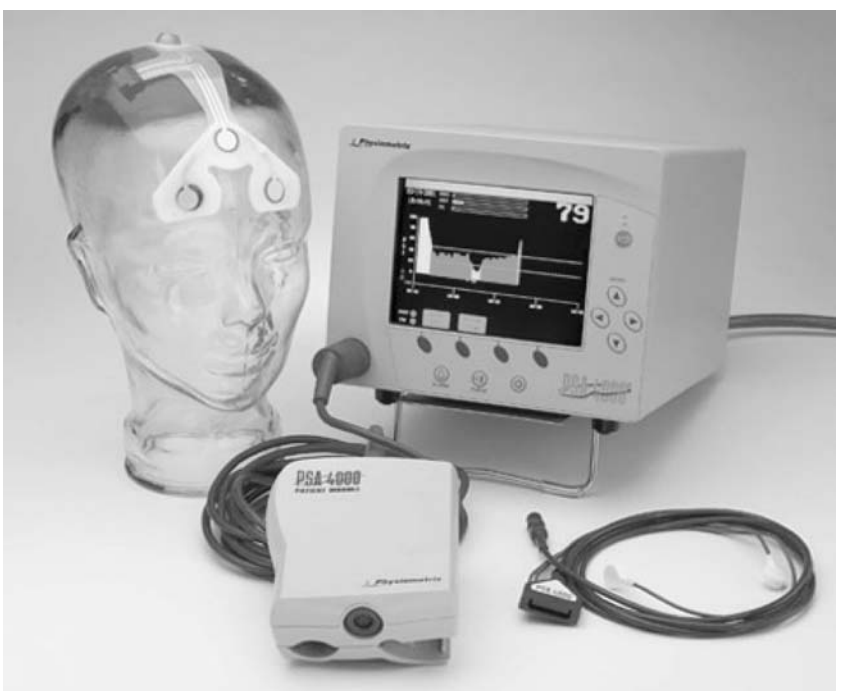


Fig. 85. Electrode position of a specially designed frontal to occipital array sensor used to monitor the level of consciousness during anesthesia.

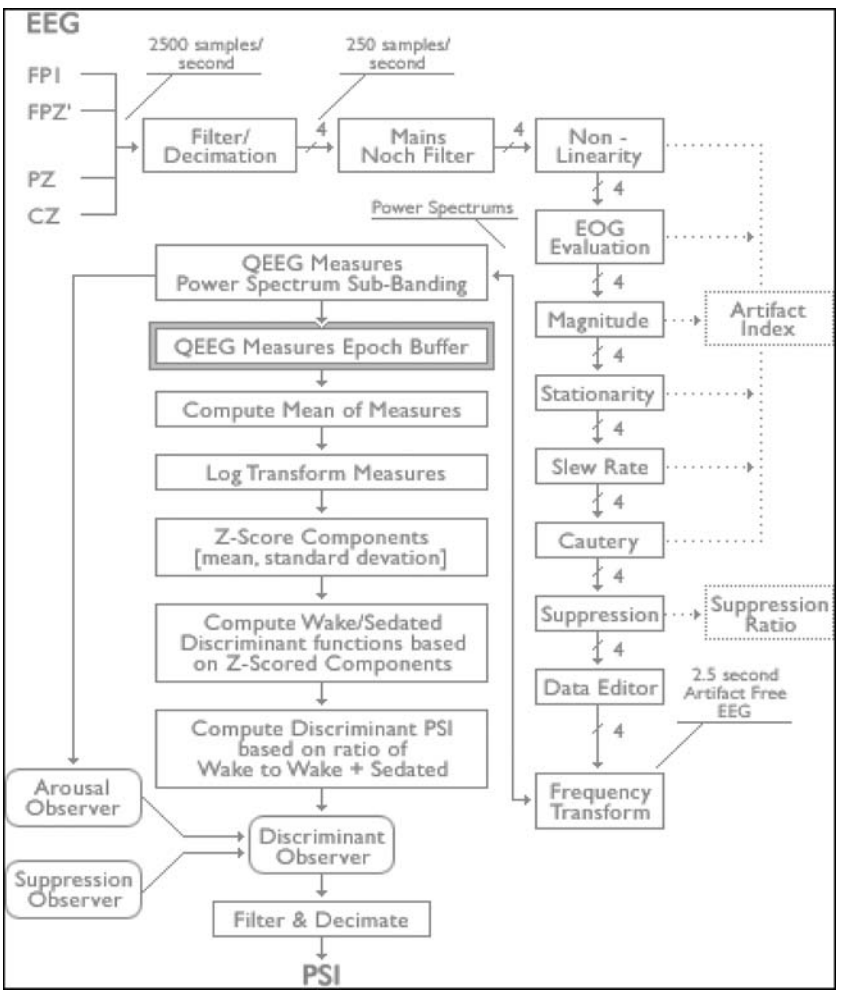


Fig. 86. The PSI algorithm, which is used to assess the patient's level of consciousness undergoing anesthesia.

b. Absolute power changes between midline frontal and central regions in beta and between midline frontal and parietal regions in alpha.
c. Total spectral power in the frontopolar region.
d. Mean frequency of the total spectrum in midline frontal region.
e. Absolute power in delta at the vertex.
f. Posterior relative power in slow delta.

All features used in the computation of the PSI are transformed to obtain Gaussian analysis as an essential step in conforming to the statistical assumptions necessary for legitimate interpretation of the multivariate statistics utilized in computation of the PSI.

Every element in the set of critical features is transformed to a standard score (Z-score) relative to its distribution in a specific reference state and expressed as the probability of deviation from that state. The current values of these standardized scores are the inputs to the constantly updating calculation of the PSI value. The PSI is the ratio of the probability that the observation belongs to the reference state versus the sum of the probabilities that the observation belongs to either the reference state or to a different level of arousal. Thus, the PSI value can range from 0 to 100.

Two "observer" functions, sensitive to the suppression ratio and to abrupt changes in level of sedation, modulate the PSI algorithm. For optimal sensitivity, these observers are 'self-normed' relative to the individual patient's baseline. These functions and the adjusted PSI are updated every 1.25 s. These updates are filtered and decimated into a sliding window, in a manner appropriate for optimal viewing characteristics, leading to an update of the global PSI trend every 6.4 s.

Hypnax® index for the assessment of the hypnotic state during sedation and anesthesia

The SomnoTrack system from Medisyst® (Linden/Germany) offers monitoring of sedation with the Hypnax® Index and graphically displays information about the depth of sleep and anesthesia. Using a 4-electrode montage with 4 channels at position Cz-C_3, T_3-C_3, F_3-C_3, and P_3-C_3, using C_3 (left hemisphere) and C_4 (right hemisphere) as the common reference. Integrated into a 10/20- cap, application is fast and easy. Results are displayed on the screen of a conventional notebook depicting the Spectral Frequency Indices (SFx), and values between 58% and 68% indicate a sufficient level of sleep, which is updated every 4 s. From the EEG cap cables run to a preamplifier with selected specificities (Figure 87).

The amplifier has a dynamic range of 0.5 μV −1 mV, picks up native EEG waves from 4 polygraphic channels with a dynamic range from 0.8 μV −1.57 mV. The sample rate is 2048 s per channel and after having passed a high pass filter (0.25 Hz; 12 dB/octave) and a low pass filter (70 Hz; 48 dB/octave) transmission rate via fiber optic coupling, data is transmitted at a rate of 128 samples/s and via a fiber optic cable to a conventional notebook. There a selective algorithm displays the hypnotic state during normal sleep and during anesthesia (Figure 88).

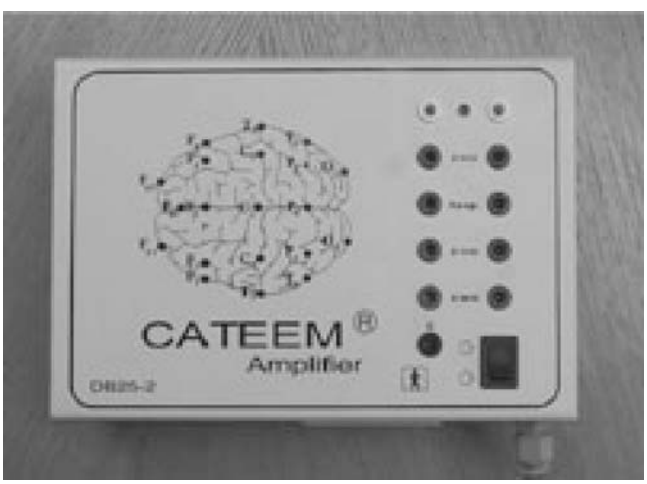


Fig. 87. The preamplifier used in the SomnoTrack system, which gathers the data of 4 EEG channels from where the Hypnax® Index is computed.

Narcotrend® – an EEG monitor to measure depth of anesthesia in the or and sedation in the icu

The Narcotrend (MonitorTechnik, Germany) is an easy-to-use EEG monitor for the automatic assessment of brain waves. Based on a number of processed EEG parameters an automatic classification of the EEG is conducted by means of multivariate statistical analysis. The classification of the EEG signal is done on an established scale proposed by Kugler ranging from stage A (awake) to stage F (very deep narcosis) [117]. The automatic classifications of the EEG over time form the cerebrogram. In this way, the user gets important information about the patient's hypnotic state in the course of time even without special knowledge of the EEG [118–120].

The automatic classification of the EEG by the Narcotrend® makes it possible to assess the patient's hypnotic state during anesthesia and sedation even for users without any specialist knowledge of EEGs.

The automatic classification of the EEG by the Narcotrend® makes it possible to assess the patient's hypnotic state during anesthesia and sedation even for users without any specialist knowledge of EEGs.

The comfortable program handling and the small, robust hardware permit the use of the system in clinical routine in the operating theatre and in the intensive care unit.

The device has been validated for total intravenous anesthesia (e.g. propofol, etomidate, thiopental, methohexital) and all common inhaled anesthetics (e.g. desflurane, sevoflurane, enflurane, halothane) [121–123] and is characterized by:

a. Extremely low running costs as conventional Ag/AgCl ECG electrodes, needle electrodes or cup electrodes can be used. There is no need for use a separate integrated electrode band

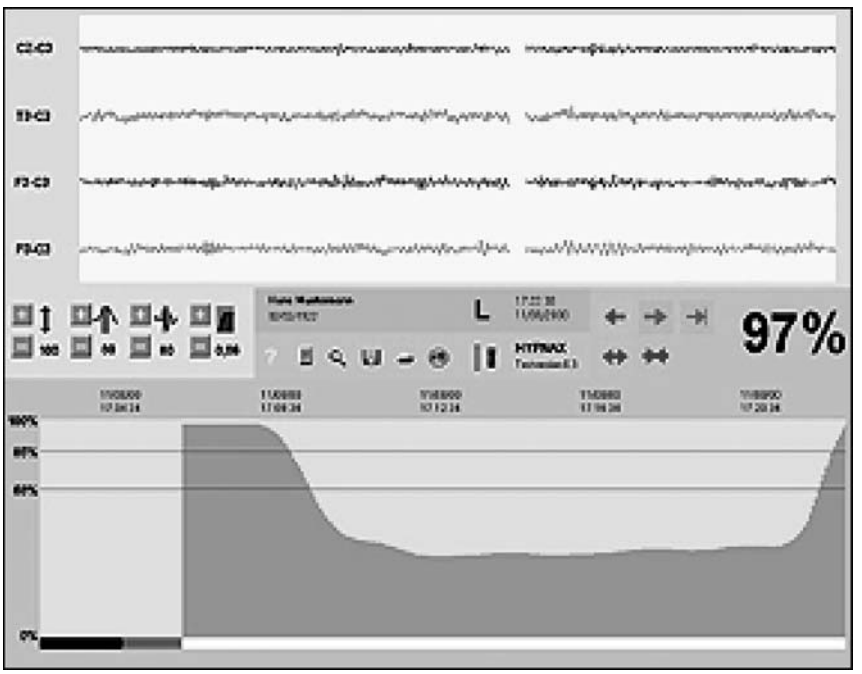


Fig. 88. The Hypnax® Index following induction of anesthesia with sufentanil starting at a value of 97% from the wake state and getting down to 45% as the patients falls asleep.

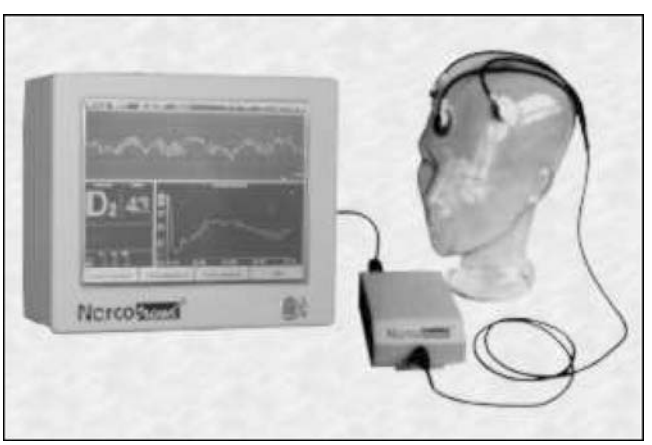


Fig. 89. Electrode montage being used in the application of the Narcotrend®.

b. 1- and 2-channel-recordings from different electrode positions possible, therefore suitable for use in all surgical disciplines (Figure 89).
c. Color display for various representations of the EEG and EEG parameters
d. Special algorithms for preventing misclassifications of the EEG during anesthesia if special patterns, e.g. epileptiform activity, occur
e. Because of its compact and robust hardware there is easy integration into the anesthesia work place
f. Simple to operate and easy operation via touch screen
g. Data transfer via serial interface possible
h. Comfortable program handling with an easy, menu-driven operation, individually adjustable scaling of diagrams plus complete storage of all data.

The Cerebrogram® has the following specifications (Figures 90 and 91).

1. Clearly arranged screen display
2. A trend display of the automatic EEG classifications)
3. The raw-EEG signal
4. The different power spectra
5. Two quantiles of the power spectrum (median and spectral edge frequency)
6. Power and cumulative representation of relative power in the standard frequency bands
7. Comparison of signals from both hemispheres
8. 1 or 2 channels registration with trend display
9. Relative power in the standard frequency bands $\delta, \theta, \alpha, \beta$
10. Comparison of signals from both hemispheres

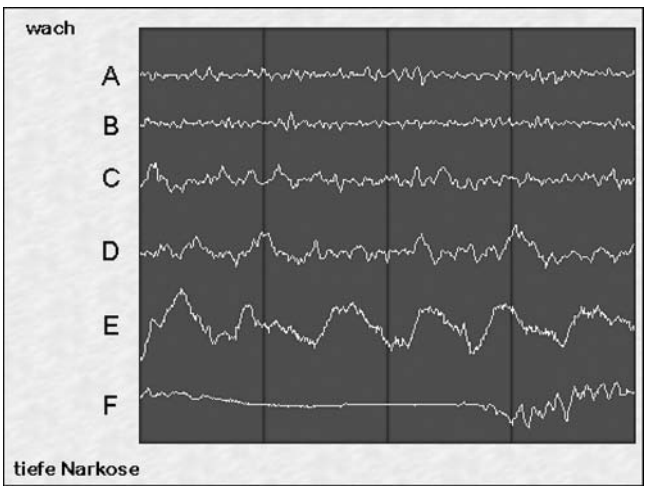


Fig. 90. The different EEG patterns as they are used for determination of sleep stages (A to F) and sedation in patients undergoing anesthesia in the OR or sedation in the ICU.

11. Trend displays on screen up to 24 h
12. Defining and setting of markers
13. 15 Hz- or 30 Hz filter and finally an
14. Automatic generation and printing of protocols

Narcotened® and Bispectral Index™ monitors have been shown to be superior for the prediction of the anesthetic state than any of the classic encephalographic parameters using probability tests [121].

The cerebral state index (CSI) a hand-held device for monitoring unconsciousness in patients

Danmeter (Danmark) has recently launched a hand-held device with the size of a cellular phone to be used at the bedside, which is able to quantify the patient's state of unconsciousness during anesthesia (Figure 92). The unit is connected via radiofrequency communication to a remote multi-parameter monitor, transmitting the spontaneous EEG via instant wireless, which does the calculation retransmitting the results to the small device at the doctor's hand.

The objective of the Cerebral State Monitor (CSM) is to scrutinize the level of consciousness during general anesthesia. The CSM displays the Cerebral State Index (CSI), which is a unitless scale from 0 to 100, where 0 indicates a flat EEG and 100 indicates the awake state. The range of adequate anesthesia is thought to be the 40–60 range, as shown in the following Table 8.

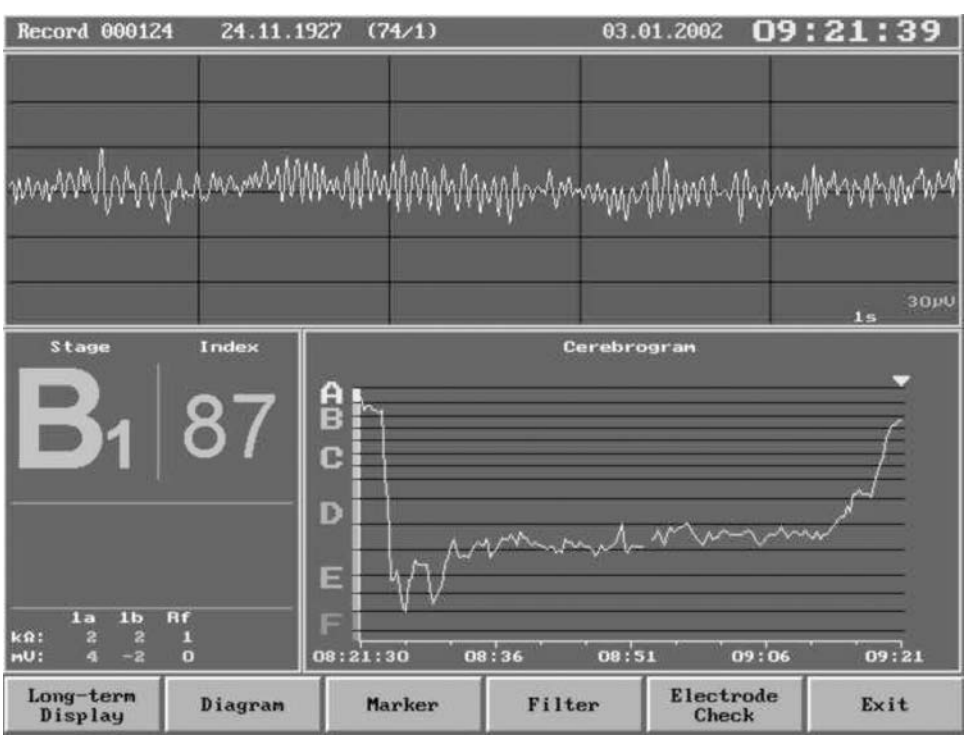


Fig. 91. Color display of the Narcotrend® monitor with the raw EEG signal, the time-related change in the cerebrogram index, and the sleep stage as originally proposed by Rechtschaffen and Kahles and further developed by Kugler for use in anesthesia.

Fig. 92. The handheld ultralight (150 g) cerebral state monitor (60 × 117 mm) determining the patients state of unconsciousness.

When CSI is below three, the EEG is practically isoelectric. The CSM requires three electrodes positioned at the middle forehead, left forehead and left mastoid. The CSM does not require proprietary electrodes. As long as the electrode impedance can be kept low, then any electrode can be used, although best results are achieved when using wet gel electrodes after proper cleaning of the skin at the electrode position, using the following montage: Middle forehead positive, left forehead reference, and left mastoid negative electrode (Figure 93). Electrodes can also be placed on the right side of the head.

For calculation of the CSI the following algorithm from the 4 sub-parameters of the EEG, the beta ratio, the alpha ratio, the beta ratio, alpha ratio, and the burst suppression

Table 9. The different cerebral state indices (CSI) used in the cerebral state monitor

CSI	Clinical state
90–100	Awake
80–90	Drowsy
60–80	Light anesthesia or sedation
40–60	Surgical plane of anesthesia
10–40	Deep anesthesia with burst of suppression
0–10	Close to coma with isoelectricity

are being used to define an index from 0 to 100. The novelty of the CSI lies in the use of a fuzzy inference system [124] in order to define the index (Figure 94).

Burst suppression (BS) is defined as the percentage of time in a 30 s window where the EEG amplitude is less than 3.5 μV. Each of the three energy ratios correlate individually to the depth of anaesthesia, but their correlation coefficients as single measures is low. This has been

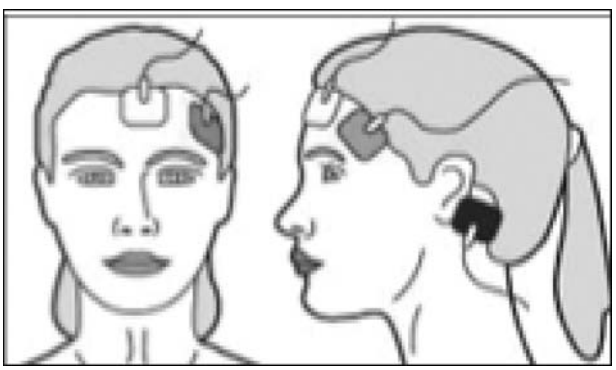


Fig. 93. Placement of snap-on electrodes on specified locations for EEG recording.

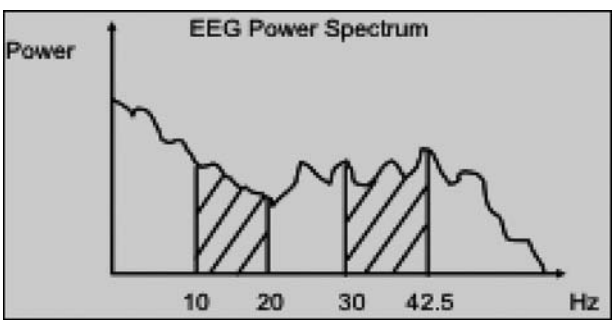


Fig. 94. The EEG power spectrum with bands being marked for the calculation of the beta ratio.

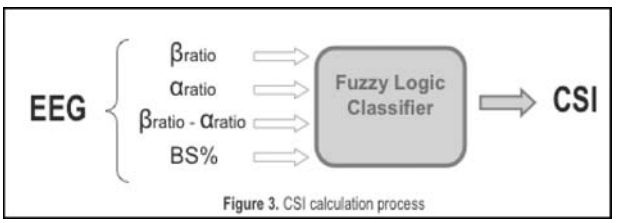


Fig. 95. The algorithm being used in the cerebral state anylyzer for calculation of the level of unconcsiousness (BS = burst suppression).

shown already by other [125]. However, by appropriately combining the parameters, a higher correlation coefficient can be reached. An intuitive explanation to this fact is that the system, as demonstratesd in the figure uses automatically the best parameter(s), meaning that when one fails then another might still be a good correlate. For example, the burst suppression parameter indicates deep anaesthesia. In this case the weight on the spectral parameters will be less because they are not good correlates during deep anaesthesia with burst suppression due to the non-stationary nature of the EEG during this situation (Figure 95)

Preliminary results demonstrated a higher correlation with plasma propofol concentration than either BIS or hemodynamic parameters [126].

Summary of guidelines for intraoperative monitoring of the EEG

The electroencephalogram can be a useful tool for monitoring the brain when surgical procedures may potentially compromise blood perfusion to the brain or involve the cerebral cortex. Computer processed EEG provides frequency analysis and data reduction of the scalp EEG, and is often used during vascular procedures. The continuous EEG, however, remains the standard for recording when pattern recognition is required, such as during electrocorticography [127]. In either case, it is essential that the monitoring technologist be very familiar with anesthetic agents and their effects on the EEG.

1. ELECTRODES

1.1 Placement The full head should be measured according to the International 10/20 System of Electrode Placement. No fewer than 21 electrodes should be applied.

1.2 Impedances all inter-electrode impedances should be between 500 and 5000 ohms. High electrode impedances or poorly matched impedances can increase line frequency inference.

1.3 Type collodion application of scalp electrodes is preferred. Sterile subdermal needle electrodes may be used when the placement of electrodes would impinge on the operative field. Modified electrode placements in surgical procedures involving a craniotomy may require modification of the standard 10/20 placement. Alternative placements should be documented and well illustrated on the technologist's work sheet. Modified placements may also reduce the number of electrodes that can be applied.

2. RECORDING CHANNELS

Eight-channel recordings can give adequate information for generalized abnormalities. To detect more localized ischemia events, however, it is recommended that 16-channel recordings be used whenever possible, with 21 channels optimal. The additional channels provide the opportunity to monitor other physiological activity such as EKG, movement, blood pressure, etc.

3. RECORDING PARAMETERS

3.1. High-Frequency Filter A high-frequency filter of 70 Hz is preferable although lowering this to 50 or 35 Hz may be necessary due to the electrically hostile environment of the operating room.

3.2. Line-Frequency Filter Line- frequency filters may be necessary, again due to the electrically hostile environment. It may be necessary to re-evaluate the application of electrodes to eliminate unwanted line-frequency (50 or 60 Hz) interference. The line-frequency filter should be used judiciously and only after all other methods of reducing 60 Hz interference have been exhausted. 3.3. Low-Frequency Filter a low-frequency filter of 0.3–0.5 Hz is recommended to best record the slow EEG activity from anesthetic agents and ischemia. Although a low-frequency filter of 1 Hz is reasonable at times, a filter of 5 Hz should be restricted to brief periods of viewing low amplitude beta activity or spikes. During procedures that can disrupt or reduce cerebral blood flow, it is important to maintain a lower (0.3–0.5 Hz) filter setting in order to record the physiological effects of cerebral ischemia.

3.3. Chart/Paper Speed. The baseline recording of the EEG should be performed with a standard paper speed of 30 mm/s. The paper speed can then be slowed to 5 to 15 mm/s to emphasize beta asymmetries and slow activity, as well as to conserve paper.

4. BASELINE RECORDING

It is recommended that preoperative and baseline recordings be performed on all patients to rule out any EEG abnormalities that may complicate interpretation during surgical or radiological procedures.

5. EEG MONITORING DURING SURGICAL AND RADIOLOGIC PROCEDURES

5.1. Carotid Endarterectomy.

This procedure is performed to remove atherosclerotic plaque from the carotid artery, which can become dislodged and result in a stroke. The carotid endarterectomy includes clamping the branches of the carotid artery above and below the plaque or stenosed area so that the material can be surgically removed. Because the clamping can produce significant cerebral ischemia, the EEG is used to evaluate collateral perfusion of the brain. The EEG monitoring should begin with the start of the surgical procedure. Once anesthesia levels are stabilized, the baseline EEG activity should be noted for reference throughout the procedure. Changes in the EEG will typically occur 30 s to 2 min after clamping of the carotid artery. The first EEG change is usually a decrease in background alpha and beta activity. Anesthetic agents that enhance fast activity actually improve the detection of this first change. The diminished fast activity should be compared to the baseline recording, and can appear over one or both hemispheres. A second indication of ischemia EEG change is increased slow activity, again with the change as compared to the preclamped baseline. Both decreased amplitude of fast activity and increased slow activity may be seen at the same time. The degree of resulting ischemia is greatest when there is a significant reduction in both fast and slow activity unilaterally or bilaterally or there is a total suppression of the EEG. The amount of disruption in the cortical activity displayed on the EEG determines the window of time for correcting the ischemia before irreversible damage occurs. Anesthetic agents can mimic some of the EEG changes described above; therefore, communication with the anesthesiologist is essential and any changes in anesthetic levels should be clearly noted on the EEG record. Alarm criteria for the technologist to alert the surgeon to significant changes should be determined by the surgical/technical staff at each hospital and established prior to surgery. (Some have established a drop of 50% in amplitude of the fast frequencies, as compared to the baseline recording, as significant.) It is of the utmost importance that the technologist be aware that both diffuse and subtle, focal change may occur caused by embolic events, which may lead to permanent neurologic deficit [128]. A physician with training in the interpretation of EEGs should be present during any procedure that requires cross clamping of an artery.

5.2. Intracranial Aneurysm Surgery

The large craniotomy necessary to expose most intracranial aneurysms limits the scalp area available for electrode placement. Silicone electrode strips, placed by the surgeon, can be used to record directly from the cortical surface. Disruption of middle cerebral artery blood flow will cause EEG changes similar to those seen during carotid endarterectomy. It may be necessary to "trap" aneurysms of the intracranial portion of the internal carotid artery with temporary clips. Placing the clip across the neck of an aneurysm can cause a pinching effect that reduces the amount of flow in that artery or causes a complete blockage. The EEG changes are very quick to appear and can guide the surgeon in repositioning the clip. Aneurysms of the more distal middle cerebral artery and the anterior circulating arteries may produce more focal EEG changes, depending on how distal they are. A physician with training in the interpretation of EEGs should be present during any procedure that requires clipping of any aneurysm.

When the involved arteries also perfuse the brainstem, the BAEP may be monitored along with the EEG.

5.3. Cardiac Bypass Surgery

Cardiac bypass procedures have been known to produce cerebral ischemia causing postoperative stroke. The monitored EEG has been used as an indicator of cerebral ischemia; however, EEG features are suppressed by the profound hypothermia often used to protect the brain. The EEG is used to identify the suppression of all brain activity to determine when hypothermia has been established, and can also be used to monitor deliberate, drug-induced burst suppression.

5.4. Electrocorticography (ECoG)

Following craniotomy, electrodes are placed directly on the surface of the brain to localize epileptiform activity in patients with epilepsy, or to isolate abnormal activity related to tumor growth or other invasive events. The cortical recordings are obtained by using strips or a grid of EEG electrodes embedded in narrow bands or rectangular sheets of silicone with an interelectrode spacing of one centimeter. These

arrays can be sterilized and applied on the cortical surface with saline-soaked cotton strips to hold the array down. Another type of ECoG electrode system employs a metal or plastic frame that holds a series of spring-loaded, cotton-tipped electrodes that touch the surface of the cortex. The spring mechanism absorbs the pulsations from the surface of the brain. This type of electrode array is more flexible for random placement of the electrodes around an area of suspected abnormality. During such monitoring, a physician with training and experience in the interpretation of ECoG must be present during the recording.

5.5. Sodium Amytal Testing (Wada Test)
The Wada test is performed prior to epilepsy surgery to determine the patient's hemisphere dominance for language and memory [129]. The EEG is used to record the slow activity induced by sodium amytal, thus giving an electrical estimate of the duration of the amytal effects and the hemispheric recovery from the drug. The EEG will also reveal any seizure activity that could compromise the test results. The Wada test is classified as an intraoperative procedure in some institutions around the world.

In regard to the usefulness of computerized EEG monitoring in the clinical environment, the bottom line message can be summarized as follows:

1. Besides the Ramsey Score EEG power spectra are useful in determining the hypnotic depth in the ICU, avoiding an over- undersedation.
2. They are useful in TIA to avoid awareness!!!
3. They are useful in patients with a compromised hemodynamic system, especially in the elderly.
4. They are useful to monitor possible malperfuson during deliberate hypotension.
5. They are useful in cardio-pulmonary bypass in detecting cerebral hypoperfusion/ischemia.

However:

6. They are not useful in determining level of analgesia during anesthesia.
7. They are only partially useful in CEA when used together with SSEP and/or TCD.
8. They are only partially useful in pharmacological studies when used as EEG-fingerprints.
9. They demonstrate little value to diagnose anesthetic overhang for the experienced anesthesiologist.
10. They are not useful in detecting ischemia in deep brain structures.

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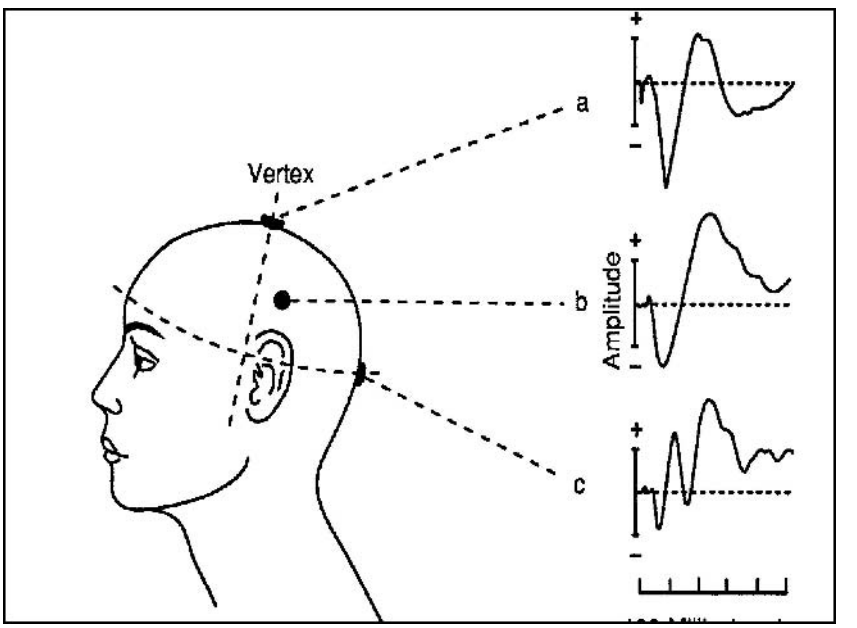
CEREBRAL MONITORING IN THE OPERATING ROOM AND THE INTENSIVE CARE UNIT – AN INTRODUCTORY FOR THE CLINICIAN AND A GUIDE FOR THE NOVICE WANTING TO OPEN A WINDOW TO THE BRAIN

Enno Freye, MD, PhD

PART II. SENSORY-EVOKED POTENTIALS (SSEP, AEP, VEP)



Author address: Clinics of Vascular Surgery and Renal Transplantation, Heinrich-Heine-University, Düsseldorf, Deichstr. 3a, 41468 Neuss-Uedesheim/Germany.
E-mail: enno.freye@uni-duesseldorf.de

ABSTRACT.
An evoked potential differs from the EEG mainly in two ways:

1. The EEG is a random, continuous signal, which arises from the ongoing activity of the outer layers of the cortex. An evoked potential is the brain's response to a repetitive stimulus along a specific nerve pathway.
2. EEG signals range from 10-200 milliVolt (mV). Evoked potentials are smaller in amplitude (1-5-20 μ Volt requiring precise electrode positioning and special techniques (signal averaging) to extract the specific response from the underlying EEG 'noise'. The technique of signal averaging, as originally described by Dawson in 1954 [69J, has been further developed in computer processing. The technique is now used by applying a stimulus repeatedly – preferably at randomized intervals – and to record the evoked response over the corresponding area of the brain, averaging out mathematically the change over the number of stimuli.

Rationale for the use of EPs in the OR and the ICU
Evoked potentials (EPs) serve the following major purposes:

1. Monitoring of the functional integrity of neural structures that may be at risk during, for instance, ECC (extracorporeal circulation) or endarterectomy indicating cerebral hypoxia.
2. Monitoring of the effects of anesthetic agents and other centrally active drugs, which, besides the cortex, affect deeper neuronal structures.
3. Orthopedic cases where the spinal cord is at risk such as Harrington rod insertion and removal.
4. Clamping of the abdominal aortic artery during aneurysmectomy resulting in a potential damage of the lower parts of the spinal cord.
5. Clipping of an intracerebral aneurysm, which may be impeding blood flow to vital cerebral textures.
6. An indicator of cerebral hypoxia when the blood pressure is deliberately lowered.
7. Operation on peripheral nerves and nerve roots to identify early trauma.
8. Monitoring the cerebral function during controlled hypothermia when the EEG becomes flat.
9. Monitoring of the pathophysiological conditions after severe head trauma and the effects of therapy.
10. An intraoperative warning device of unsuspected awareness during light anesthesia when movement is abolished by muscle relaxants and cardiovascular responses are modified by vasoactive drugs.

The principle of the method is to apply a stimulus and then to record the electrical change of the signal along its specific pathway up to the corresponding region of the brain. The stimulus may be of either visual, auditory or of somatic nature.

In case of the latter the stimulus is a small electrical potential applied to the skin of the hand. Thereafter, the stimulus travels along the specific nervous pathways inducing (= generating) potential activation at various sites. The generation of potential changes at various sites along the pathway is an index for the integrity of the nerve. Thus, the evoked potential can be considered a neurophysiological response (usually of the cortex) to impulses originating from some externally stimulated sensory nerve. They provide a physiological measure of the functional integrity of the sensory nerve pathway, which can be used as a clinical diagnostic tool as well as for intraoperative monitoring. The evoked potential usually is recorded from the specific cortical area corresponding to the stimulus input.

The classification of evoked potentials
Stimulating a sensory nervous pathway induces evoked potentials. If the auditory nerve is stimulated by 'clicks' from headphones, it is called the auditory evoked potential (AEP). The early part of the AEP waveform (less than 10 msec) is called the Brainstem Auditory Evoked Potential (BAEP) since it reflects the passing of the impulse through the brainstem.
If a nerve on the arm or the leg is stimulated by a small electrical current applied to the overlying skin, it is called the Somatosensory Evoked Potential (SSEP). If, however, the retina is stimulated by means of flicker light or a sudden change in a checkerboard pattern, the evoked potential thus recorded over the corresponding cortical area is called the Visual Evoked Potential (VEP). Evoked potentials are used both as a diagnostic tool and as a monitoring technique. As diagnostic tests, evoked potentials are useful to evaluate neurologic disorders such as:

a) multiple sclerosis,
b) acoustic nerve tumors, and
c) optic neuritis.

As a monitoring modality, evoked potentials are used during all surgical procedures, which might compromise part of the brain or the spinal cord.

KEY WORDS. somatosensory evoked potential (SSEP), acoustic evoked potential (AEP), visual evoked potential (VEP), AAI index, anesthesia, intensive care algesimetry

INTRODUCTION: REASONS TO MONITOR EVOKED POTENTIALS

Sensory evoked potentials present a neurophysiologic procedure performed to assess the integrity of both cranial and peripheral nerves during surgery. The procedure monitors nerve function by activating or stimulating a nerve or group of nerves primarily to observe the contractions of the muscle groups affected by the stimulation of a nerve or particular group of nerves. Intraoperative monitoring of somatosensory evoked potentials (SSEPs) is used during orthopedic or neurologic surgical procedures to reduce

surgically induced morbidity and/or to monitor the level of anesthesia. SEP are electrical waves that are generated by the response of sensory neurons to stimuli. Changes in the electrical waves are averaged by a computer and then interpreted by a physician. The SEPs can then be used to assist the diagnosis of certain neuropathologic states or to provide information for treatment management.

A. Intraoperative neurophysiological monitoring may be cost-shared during surgical procedures that could potentially cause harm to the brain, spinal cord or peripheral nerves. Visual, auditory, and somatosensory evoked potential recordings are considered eligible for financial coverage for the following indications:

1. Visual evoked potentials (VEP).

    a. To diagnose and monitor the acute and chronic phase of multiple sclerosis.
    b. To localize visual field defects occurring in the absence of structural lesions, acquired metabolic disease or infectious disease.

2. Auditory evoked potentials (AEP).

    a. to evaluate brainstem function and metabolic disorders;
    b. to identify the presence of brainstem tumor when MRI or CT is ineffective or unavailable;
    c. to diagnose and monitor demyelinating or degenerative brainstem diseases, such as multiple sclerosis, central pontine myelinolysis and olivopontocerebellar degeneration;
    d. to diagnose the presence of lesions in the external auditory system, such as acoustic neuromas;
    e. to assess recovery brainstem function after removal of space occupying lesions compressing the brain stem;
    f. to supplement the EEG in evaluating brain death or irreversibility of coma; and
    g. to measure the type and extent of hearing impairment or determine the degree of neural maturation in neonates, infants, and children less than five years of age.

3. Somatosensory evoked potentials (SSEP).

    a. to assess somatosensory function in unconscious patients who have sustained traumatic damage to the spinal cord which is demonstrated by radiologic examination and who are candidates for emergency surgery of the spinal column,
    b. to diagnose and manage suspected space occupying lesions or demyelinating and degenerative diseases in the somatosensory system not identified by radiologic examination,
    c. to monitor large tumors which may cause significant brainstem compression or ischemia (deficiency of blood supply),
    d. as an indicator during operations when surgical intervention/ manipulation puts the spinal cord at risk (e.g., sclerosis surgery, resection of spinal arteriovenous malformations, removal of intraspinous tumors and some cervical discectomies);
    e. to monitor surgery during intracranial aneurysms; and lastly
    f. to monitor a sufficient depth of analgesia.

BASIC PRINCIPLES IN EVOKED POTENTIAL MEASUREMENTS

What is an evoked potential

An evoked potential is an electrical by-product of activity in peripheral and central neural pathways in response to an external stimulus.

The advantages of recording evoked potentials are:

(a) Obtain functional information about specific, neuronal structures,
(b) Measure objectively nerve activity,
(c) Use a non-invasive technique,
(d) Perform a rapid and simple procedure.

The evoked potential is useful for:

(a) Demonstrating normal nerve function,
(b) Detecting abnormal nerve function,
(c) Localizing a problem to a segment of the conductive pathway of a nerve,
(d) Characterize the severity of a problem.

Contrary, the evoked potential is not useful for:

(a) Giving psychophysical information from higher centers in the brain,
(b) Giving absolute normal/abnormal answers, since the results are statistical derivations,
(c) Characterizing the type of pathology causing an abnormal response.

Evoked potentials have the following characteristics:

(a) They have a low amplitude (0.1–20 μV),
(b) They have a short (generally $<$50 msec), and a long (generally $>$100 msec) latency,

(c) They are buried in noise, which originates from both outside (exogenous noise) and inside (endogenous noise) the body.

When measuring evoked potentials a signal is derived. The signal is defined as nerve activity associated with reception, transmission, and processing of a stimulus. The derived signal relates to electrical activity at the scalp, which relates directly to processes in nerve cells and fiber tracts. Several factors have to be considered when the activity in neural "generators" move to scalp fields as they are picked up by the recording electrode:

1. The activity in nerve fibers is related to membrane events.
2. The activity depends on local electric field characteristics.
3. Currents activity is transmitted from cortical layers through fluid, the skull, and the skin of the scalp where it is picked up by the electrode.

Nerves have electrical fields associated with their activity, where charged ions are actively moved across the nerve membrane to create a potential difference between the interior and exterior of the axon (<75 mV neg. inside). When an action potential is generated the potential is briskly and locally reversed. Regions of positive and negative charges are separated along the surface of the neuron (the generator). As the stimulus travels along the nerve, a transient electrical field is set up obeying Coulomb's Law ($E = Q/R^2$) where the field strength is proportionate to the amount of charge and inversely proportional to square of distance from charges. As a result transient current flows between separated charges.

At the cortical surface, electrical field intensity and gradient are determined by distance and orientation of the source: Near field vs. far field evoked potentials (Figure 1).

The near-field potential is characterized by a small spread and a steep gradient, while the far-field potential is characterized by a wide spread and a shallow gradient. The evoked neuronal response has to be transmitted through cerebrospinal fluid, membranes covering the brain (dura, pia mater), the bony skull, and the scalp resulting in diffusion of the potential, causing decreased amplitude and a blurred spatial distribution (Figure 2).

In evoked potential recording the chain is reversed, projecting back from scalp activity to the neural generator. However, there are a number of complicating factors like multiple sources where the fields from different generators overlap each other, adding in time and space, making an individual contributions of generators difficult or sometimes impossible to distinguish. In addition, for reasons of difference in fiber length, synchronicity and geometry,

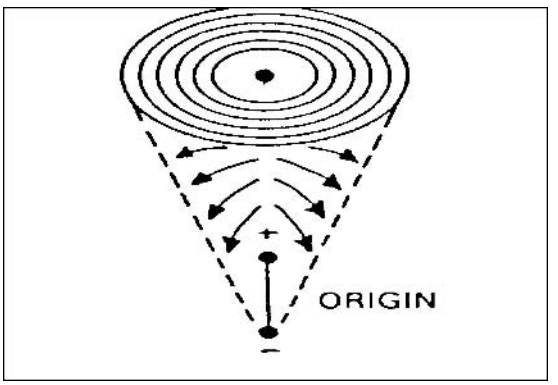


Fig. 1. Schematic drawing of generation of far-filed evoked potentials.

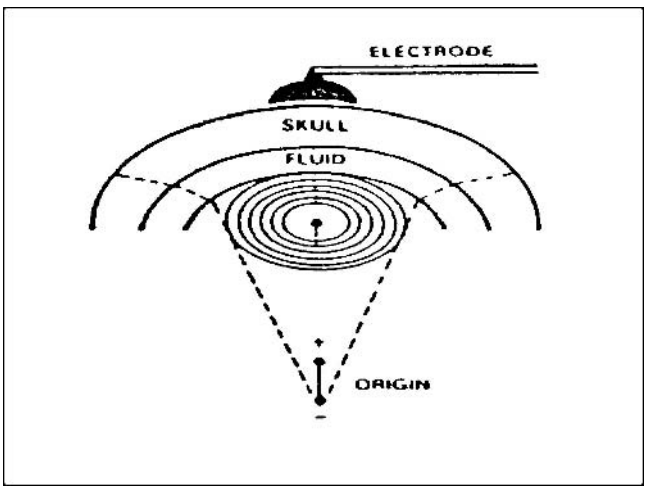


Fig. 2. Schematic drawing of transmission of the evoked potential through the different layers of the skull.

there are open and closed fields, so that not all nerve activity generate external fields. Presently the knowledge what we know about human brain is not enough, and animal models offer limited help. Also, it is not known whether axons or dendrites act as primary generators. In the cortex the generators have different orientations, sizes and time courses of activity in different individuals, so that one can only approximate generator location. But, that's enough to identify the source of damage, since the brain is small and for instance in Brain-Stem Evoked Potential Recording (BSEP) it is insignificant if the generator of wave V is in the lateral lemniscus or inferior colliculus. Both areas are physically less than 1 cm apart, an insignificant distance from the clinical viewpoint.

What does a normal evoked response tell you?

1. The sensory stimulus was transduced and conveyed to the brain.

2. The nerve activity arising from the stimulus reached certain landmarks at certain times.
3. The time of arrival signifies conduction speed.
4. The duration of evoked potential can be related to synchronicity of nerve firings.
5. The amplitude of the evoked potential is influenced by the number of fibers firing at a given point in time.

What does an abnormal response signifies? It tells you that the stimulus was not transmitted due to:

(1) Pathology or interruption within the pathway
(2) The response was not recorded because of

(a) Poor electrode contact
(b) Too much noise
(c) A technical problem.

In evoked potentials testing, always strive to optimize results: Make the signal as large as possible, and make noise as small as possible.

BASIC TECHNOLOGY IN EVOKED POTENTIAL RECORDING

The importance of avoiding electrical noise in evoked potential recording

Noise is comprised of all other electrical activity other than the desired signal, which is picked up by the recording electrode. The objective is to minimize the noise before it gets into the recording instrument. The other and less desirable step is to reduce noise after it has gotten into the instrument using filters, signal averaging, etc.

Generally speaking there are different types of noise; asynchronous noise, which is not locked to a stimulus and can be differentiated into:

(1) **Exogenous noise** from the environment such as motors, lights, x-ray machine, TV fields, sounds (talking). The solution is to remove the exogenous sources from the recording area and keep electrode impedances low.

Another possibility to reduce ambient electrical noise is the use of a 1 KΩ resistor active-to-reference jumper connection and move reference to ground electrode. Also, move the preamplifier around to various positions while observing noise in the EMG mode until noise is avoided, widen the filter setting, and finally position the machine (and patient) away from noise. Check to make sure that the third wire electrical ground is really ground and neutral. Faraday screens are not really necessary. Once they are used, one has to make sure that they are installed correctly.

(2) **Endogenous noise** arising within the patient such as the EEG, the EKG, the EMG, blinks, or muscle twitch. The solution is to keep electrodes away from these sources of noise in the patient, by relaxing the patient, keeping the impedance low, and lower stimulus intensity.

(3) In addition, there is **synchronous noise**, which is locked to the stimulus such as exogenous 60-cycles and/or stimulus artifacts. The solution is to remove the sources of such noise by changing the repetition rate so it is not a multiple of 60. Ideally, a random stimulation rate should be chosen if possible. Also, the stimulus intensity should be lowered.

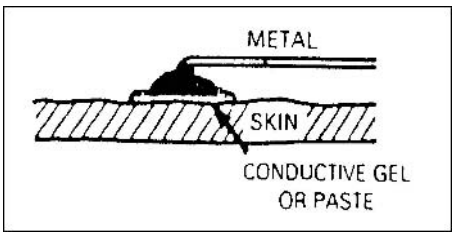


Fig. 3. The critical connection of the electrode with the skin.

Current only flows through electrodes to the extent that this path offers less resistance than the skin path. Therefore, one must minimize electrode impedance at the electrode connection to the skin (Figure 3).

The following steps are recommended in order to reduce resistance between skin and electrode, since high impedance heightens noise pick up.

1. Remove dead skin from recording surface by using an abrading gel (Omniprep™). In addition one should remove perspiration and oily skin as this spreads the potential, decreases the amplitude, and increases artifact by using alcohol. And lastly conductive gel or paste should be applied to the skin beneath the electrode to reduce resistance.
2. Tape the electrode firmly to the skin surface so that it doesn't move and that paste or gel beneath the electrode doesn't dry out.
3. Use the impedance meter and adjust the connection of the electrode to the skin so that the impedance levels

are at 3 KΩ or less. Balance the impedance levels for all electrodes as much as possible.
4. Make sure that the active to reference electrode has the lowest path of resistance.
5. Balance the impedance levels for all electrodes.
6. Electrodes act as antennas for tiny electromagnetic waves in air, and generates random noise themselves. Therefore, all electrodes should be made from same metal to avoid AC potential.
7. Place the recording electrode as close to the source of the evoked potentials as possible, since the amplitude is proportional to $1/R^2$.
8. The ground electrode is used to improve the ability of the amplifier to reject noise, if lowest impedance levels are maintained, and when it is located near the stimulation site. Ground is not a signal path and ground is not an earth ground!
9. The leads of electrodes act as conductors. Think of them as antennas. They should be kept as short as possible, they all must have the same length, they must follow the same path to the amplifier, they should be kept away from all potential sources of noise, and lastly they should be checked for an unbroken protective insulation at any point.

The differential amplifier – what it is, how it works and why it is necessary in evoked potential recording

The differential amplifier amplifies the difference between active and reference electrodes, and rejects similarities between active and reference input using the common mode rejection ratio (CMRR) typically 100 dB (Figures 4–8).

Also, the differential amplifier directs the positive signal at active input downward on the display, and directs the positive signal at the reference input upwards on the display.

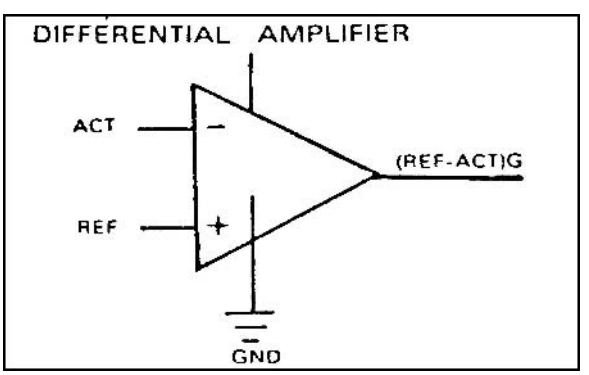


Fig. 4. The differential amplifier an integrated part in evoked potential monitoring.

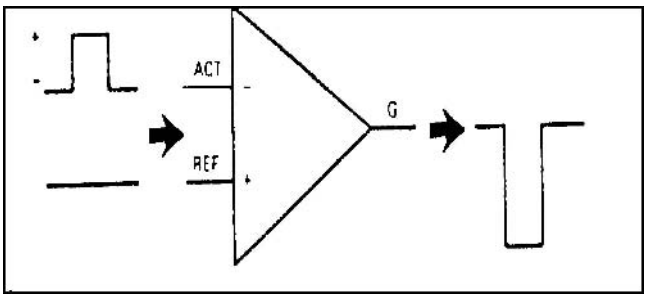


Fig. 5. Example for monopolar amplification of signal.

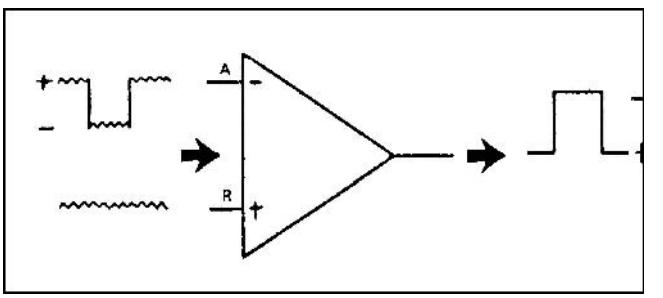


Fig. 6. Example for removal of electrical noise.

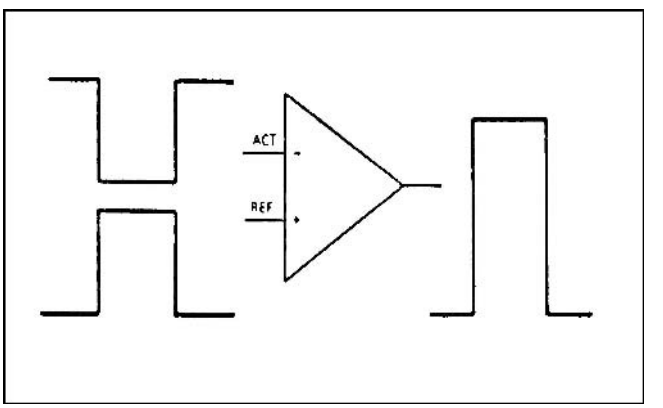


Fig. 7. Example for differential amplification of a signal.

In order to optimize noise rejection:

(a) Lower impedance of electrodes
(b) Balance impedance levels between electrodes
(c) Evaluate the choice of montage
(d) Select appropriate amplifier gain for signal.

Filter setting necessary to remove noise

Removing noise and interfering signals from the evoked response is done internally by filter settings. In the figure

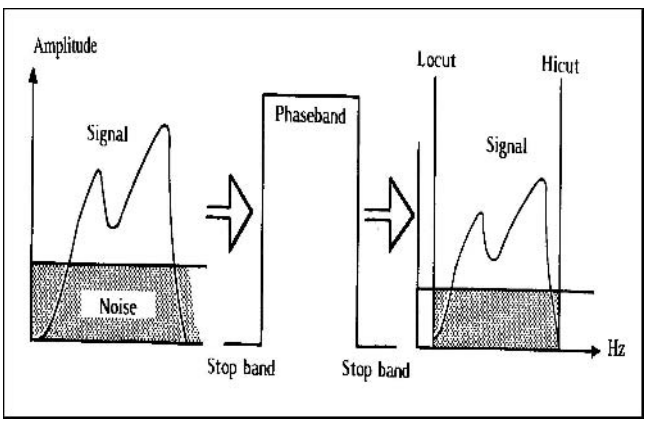


Fig. 8. The basic principle in optimization of signal-to-noise ratio using a low- and a high-cut phase band filter.

below noise is "black," containing a random mixture of all frequencies, whereas evoked responses contain only select frequencies. Therefore, the objective in filtering is to remove noise, which doesn't overlap the signal by blocking it from entering the computer system for further analysis.

The sharp edges shown in the figure are those frequencies where noise is attenuated. The filter system in reality, however, has a gradual slope as depicted in the following Figure 9.

If frequency of the filter is set at 100 Hz (fc = 100 Hz), noise is still 1/4 as large at 50 Hz. Noise therefore is not totally eliminated by filtering since an increase in the slope of attenuation introduces artifacts such as wiggling in the baseline. Filter limits are determined to analyze the pure signal by fitting high-cut and low-cut filter, surrounding the actual signal. If filters, however, remove part of the evoked potential signal, its latency and morphology will change (see Figure 9).

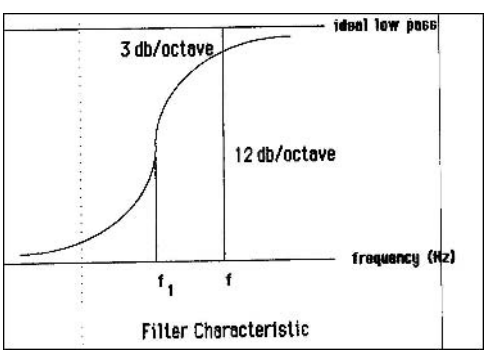


Fig. 9. The principle of the gradual slope of a low pass filter, necessary to remove noise.

The quality of the signal is related to its analog-to-digital conversion. Such process of digitization is described best by the sequence sample, hold, digitize, and latch. In discrete steps of time, samples fast enough so as not to miss an event, using 512 points per sweep, and setting up the duration of a sampling period, so that the potential fills the sweep and every component of interest appears on the screen. In discrete steps the amplitude increases, using enough steps to make all changes smooth. In general 8 bits = 256 steps are used. Allocate steps as widely over the signal range as possible, and adjust the gain control on the amplifier so that the wave fills 1/4 or 1/2 of the screen.

The averaging process, a computerized process necessary to reduce noise

Despite all efforts (reduction of noise from the environment, common mode rejection ratio, filter settings), some noise is similar to the signal so that it gets into the recording process. If noise is similar to signal frequency, it cannot be eliminated without eliminating part of the EP signal. Also it is big enough to obscure the evoked potential signal. Therefore signal averaging is used to reveal the actual event-related potential. However, one has to be aware of the following assumptions and limitations. Assuming that the signal is present and stationary, and that noise is random and asynchronous, averaging preferentially removes noise as the square root of "n" (or: $\sqrt{n}$), where "n" is the number of samples. The limitations of a signal averaging are:

(1) Noise can never be reduced to zero, only by the square root of the number of samples.
(2) Changing evoked potential signals are smeared by averaging.
(3) Synchronous noise appears as a signal.
(4) Errors within the computer can accumulate with averaging.

How much averaging is enough?

Using the theoretical approach: If one assumes that input data consists of 10 μV of noise and a 1 μV of the signal, one want to reduce to 0.1 μV noise and obtain a 1 μV signal in the sample. Performing the following analysis to determine how much averaging is enough:

Signal/Noise $\times \sqrt{n}$ = number of averaging
$10/1 \times \sqrt{n} = 0.1$ sweeps, when wanting to change to
$100/1 \times \sqrt{n} = 10.000$ averaging is necessary.

Applying the practical approach: Average as many times until the signal stops changing on the screen and stabilizes. Replicate the results to assess consistency.

Use of Enhancement Techniques when displaying the evoked response

1. *Artifact rejection* is useful for removing signals that exceed a preset maximum, as it is likely to contain excessive noise. Commonly, such a maximum is 95 percent of full scale. The advantage of artifact rejection is that it makes averaging more effective by admitting only low-noise signals. The disadvantage to artifact rejection is that it might selectively reject only particular kinds of events. For example, removing all myogenic responses or rare fraction responses from alternating clicks.
2. *Scaling* (or increase in amplitude) is useful for expanding the vertical size of the waveform. The screen amplitude equals the gain/scale factor. For example: When a 10 μV/division is changed to 2 μV/division the scaling factor is 5. However, scaling does not make up for poor gain settings, and the resolution is set by the analog-to-digital conversion. There is a maximum setting for scale factor. If this is not enough the gain setting has to be readjusted.
3. An additional feature is *smoothing* the evoked signal. This is used when one wants to remove high-frequency artifact by adding 3 points together and putting an average in the middle. Like lowering the high-cut filter, smoothing removes peak sharpness with noise. There is no change in latency shift due to smoothing.
4. *Addition* of one trace above the other is another aspect that combines traces after replication. It further lowers noise by a factor of .707.

No post-processing is as effective as taking care prior to signal acquisition. Always strive to optimize stimulus and recording parameters for the potential you are studying prior to gathering evoked potential data.

What to evaluate in the evoked response

By definition a response is a wave whose replicable peaks are seen and which are absent in a silent control run. When evaluating the response in the evoked potential, three stages are involved:

1. The control trial: Set the recording machine to parameters, which will be used in the test. Then unplug the stimulator and collect and replicate a control trial:

   (a) Noise should average to a flat line.
   (b) If not, search for source of synchronous artifact.

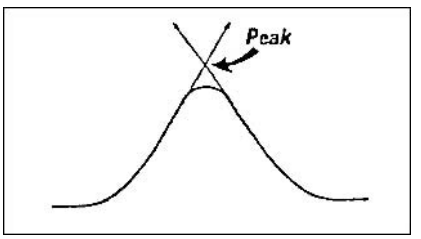


Fig. 10. Measurement of the peak of an evoked potential taking into consideration the ascending and descending slopes.

   (c) It gives a picture of "response" in the absence of a stimulus with ±average gives an alternate measure.

2. The collection of an evoked response: Plug in the stimulator and collect the evoked response. Store the evoked response collect another evoked potential in order to evaluate its replicability looking for the following features within responses:

   (a) Do the peaks line up?
   (b) Are the amplitudes similar in height?
   (c) Are peaks present, which were absent in the silent control?
   (d) Is there any variation between responses? If the response is not replicable, it is not a true evoked signal.

   Note: Complex, composite responses may add to form a signal response, or may be subtracted to compare with silent control.

3. What to measure in the evoked response.

(a) The **morphology** of peaks, are they in proper arrangement, and what is the gestalt or "feel" of the wave shape.
(b) The **latency**, where absolute and interpeak latencies represent conduction velocity to and between generators. Measure the highest point in the waveform, which reflects peak latency. More complex measurements of a peak are done at its intersection using the ascending and the descending slope (Figure 10).
(c) The **amplitude**, which is absolute, measured from baseline and its ratios. The amplitude height is related to the number of fibers and their firing synchronicity. Do an intra-subject comparison as an own control by determining any difference between left and right, and correctly for global, metabolic variables.

Detection of a pathology in evoked potential measurement

A pathology is obvious when there is a difference between subject parameters and normal parameters. Because evoked

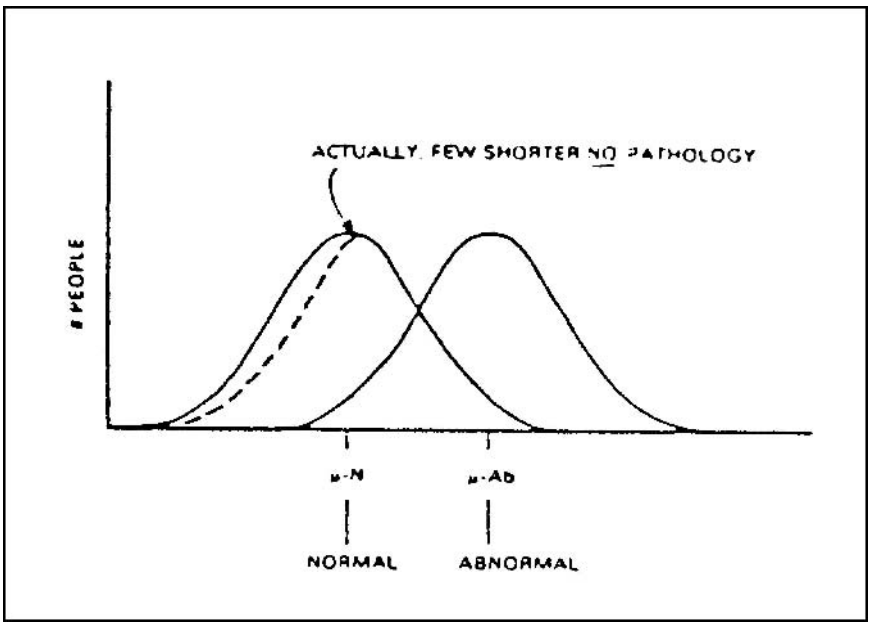


Fig. 11. Representative example when to detect a pathology in the evoked potential, where normal ±1 SD reflects 65%, mean ±2 SD reflects 95%, mean ±2,5 SD reflects 98% and mean ± 3SD reflects a 99% change.

potentials are a statistical measure, typically only a ±3 standard deviation from normal will demonstrate a pathologic condition (Figure 11).

Before doing so establish normal data with the instrument and within the environment where measurements will be done in the future.

Why should one collect normal data?

Get a set of normal responses with the equipment in the OR and the ICU environment. Verify that all procedures are correct in relation to others. Learn how to work with the equipment in the specified area in order to evaluate a potential electrical interference. Establish norms for special groups or protocols where literature norms don't exist.

How to collect normal data?

Find 10 normal people and decide on the protocol and the equipment. From thereon stick to it henceforth, because any changes will require new norms. Run the normals, find mean and deviation and compare them with data in the literature [1]. For comparisons in the future, keep the normal and the verified abnormal to expand your own database.

The normal values other than your own can be used as a guide if they match closely and they can be used for either comparison. It is always better to use your own norms than someone else's of uncertain origin and with vague correction factors. When running BSEPs and SSEPs, it's OK to follow another's normative data if his base closely matches your own clinical population. Whereas using norms of VEPs, one should exercise caution for there are too many variables, which can affect the norms in VEPs.

In summary when evaluating for normal and abnormal results, the quality of the answer depends on the specificity of the question. Caution not to over-read results, and know the place of the evoked potential test in relation to the rest of the diagnostic scheme. Minimizing one error makes the other larger, overlap is a region of uncertainty, know that evoked potential are a statistical measure, and typically use 3 ± SD when evaluating a pathology.

SOMATOSENSORY EVOKED POTENTIALS

Somatosensory Evoked Potentials (SSEPs) are a noninvasive measure of function in the pathways mediating somatic sensation between the peripheral cutaneous receptors and the primary somatosensory cortex. In general the SSEP evaluates pathways and they show the arrival of the nerve volley at specific landmarks along the sensory pathway, allowing interruptions and delays to be detected and localized. Usually SSEPs are performed on large mixed nerves of the upper and lower limbs: median and ulnar nerves in upper limbs, tibial and peroneal nerves in lower limbs. SSEPs can monitor other peripheral nerves, such as trigeminal, pudendal, and dermatomes. Additional and special techniques can be used to isolate specific nerve populations

such as cutaneous mechanoreceptors, muscle afferents, and pain fibers.

The physiology of nerves in a mixed nerve

There are different types of nerves with different conduction velocity and different types of tasks (Table 1).

Somatosensory evoked potentials mainly arise from group II fibers. Few fibers of group I fibers project to the cortex and groups III and IV are hard to trigger.

In order to elicit a somatosensory evoked response from the median nerve or the posterior tibial nerve, usually an electrical stimulus with a duration of 100 μsec, intensity of 5–30 volts and a constant current between 5–30 mA is used. The classification of the response is that at sub-threshold levels no axons fire, while at threshold levels some axons fire. Using sub-maximal level more axons fire, and at maximal level all axons fire. Voltage and current necessary for each level vary greatly from one individual to the other. Sub-maximal motor stimulation is usually enough to fire all of the sensory axons. Therefore it is only necessary to elicit a visible, but not maximal, motor twitch. The most important considerations for adequate stimulation are locating the stimulator over a large nerve, and eliciting a motor response.

If the stimulus intensity is too high it may result in an artifact where the electrical pulse will jolt the amplifier input, causing it to saturate. After saturation it may take from 2 to 10 msec to recover, depending on amount of overload and filter settings. In order to avoid stimulus related artifacts, isolate the stimulus site from the recording electrodes using a transformer in the instrumentation. In addition, keep the stimulator away from the recording leads. Another precaution is cleaning the site of stimulation so one needs lower intensities by removing perspiration from the stimulation area, keeping the electrode and the stimulator impedances low. Also, keep recording leads away from the stimulator cable, and place the ground between stimulator and recording leads.

Table 1. Summary of different types of nerves in a peripheral nerve all of which are activated in somatosensory evoked potential stimulation

Sensory group	Conduction velocity	Subserves
I	70–120 msec large myelinated	Primary muscle spindle
		Golgi tendon organ
II	40–70 msec medium, myelinated	Secondary muscle spindle, joint receptor of cutaneous
		Mechanoreceptor (discriminative)
III	5–15 msec small, myelinated	Generalized touch, prickly, pain (discriminative)
IV	0.2–2.3 msec small, unmyelinated	Deep pain, thermal sensation

The different peaks in somatosensory-evoked potentials

The first response is at Erb's Point with peak N_9 originating in the brachial plexus. It is commonly used as a reference point for measurements of central conduction velocity (Figure 12).

The montage for peripheral nervous system measurements is a dual channel recording where

Channel 1: Cz′ – Erbs Point and
Channel 2: Cervical spine CVII – Fz with grounding at the elbow Recording

The montage for central nervous system measurements is a four channel recording where

Channel 1: Erbs Point – Fz
Channel 2: Cervical spine CVII – Fz
Channel 3: Cervical spine CII – Fz
Channel 4: Cz′ – Fz with grounding at the elbow

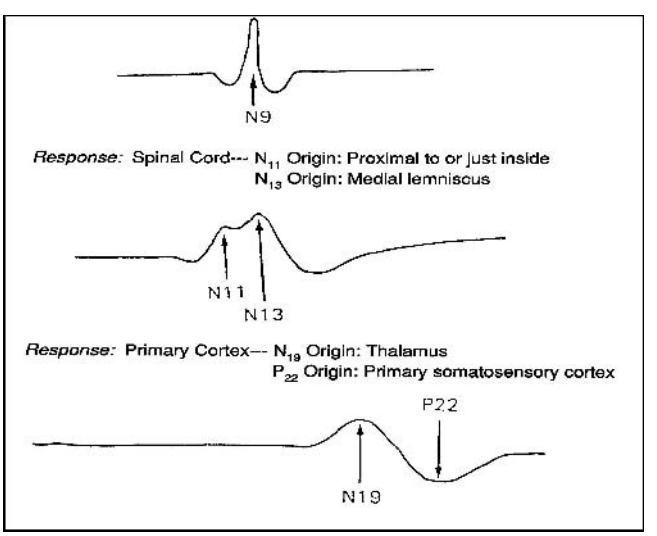


Fig. 12. The first sensory-evoked potentials as they are recorded in median nerve stimulation.

Table 2. Normative data of somatosensory evoked potentials of the median nerve. Adapted from [2]

Amplitude (μV)		Mean	S.D. (msec)
ABSOLUTE VALUES	EP	9.7	0.8
	N13	13.5	0.9
	N19	19.0	1.0
	P22	22.0	1.3
INTERPEAK	EP-N13	3.8	0.5
DIFFERENCES	EP-N19	9.3	0.5
	N13-N19	5.5	0.4
LEFT-RIGHT	EP	0.2	0.2
DIFFERENCES	EP-N13	0.2	0.2
	EP-N19	0.2	0.2
	N13-N19	0.3	0.2

Latency (ms)	Erb	C_7	C_2	N_{20}
Mean value ± SD	10.2 ± 0.9	13.5 ± 0.9	13.7 ± 0.9	19.3 ± 1.2
Upper limit (mean ± 2.5 SD)	12.4	15.8	15.9	22.3
Maximum right-left difference	0.7	0.7	0.7	1.1
Latency interval (ms)	Erb/C_2	Erb/C'_3; C'_4	C_7/C_2	C'_2; C'_3–C'_4
Mean interval ± SD	3.4 ± 0.6	9.0 ± 0.8	0.2 ± 0.2	5.8 ± 0.6
Maximum interval (mean ± 2.5 SD)	4.9	11.0	0.6	7.3
Maximum right-left difference	0.6	0.7	0.6	1.0
Amplitude (μV) base to peak				
Mean value ± SD	3.7 ± 2.3	1.6 ± 0.7	1.6 ± 0.7	2.3 ± 1.0
Range	0.8–12.3	0.4–4.1	0.4–3.9	0.6–5.3
Side difference (%)	48	36	38	46
Amplitude quotient	Erb/C_7	C_2/C_7	C'_3; C'_4/C_7	
Mean	2.3	0.98	1.4	
Range	1.1–8.8	0.7–1.7	0.7–8.9	

Recommended equipment setting is as follows:

Gain = 10 μV/Division
Sweep = 5 msec/Division
Scale Factor = 2
Repetition Rate = 2.11–4.22/sec
High-cut filter = 2000 Hz
Low-cut filter = 10 Hz
Pulse duration = 10 μHz
Artifact rejection = on

If the waveform is unclear, increase the stimulus intensity slightly, decrease the repetition rate, and lastly check electrodes and instrument settings. If there is too much noise increase number of averages, relax the patient and if sedation is required use 10 mg diazepam p.o. at pre-test. For comparison use normative data (Table 2) as published by Chiappa [2].

The following non-pathologic stimulus factors can alter the evoked response:

(a) The **mode of stimulation**: There is a better response on electrical than tactile stimulation.
(b) The **stimulus Intensity**: There is no change in latency, however, the amplitude increases as the intensity of the stimulus increases until the thumb twitches; there is no further increase afterwards.
(c) The **repetition rate**: As rate increases, amplitude decreases. A rate of below or at 5/sec (5 Hz) is best. There is no significant latency change with repetition rate.
(d) The **filter setting**: Since the response is in the range of 25 to 2500 Hz, the Low-cut filter should not be higher

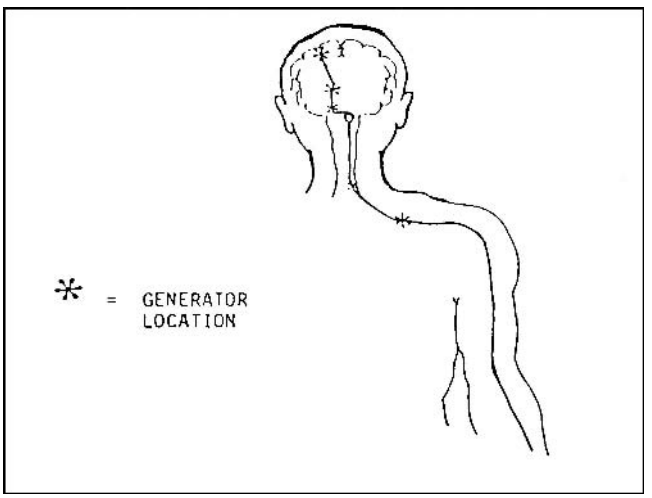


Fig. 13. Generator location of in median evoked somatosensory-evoked potentials.

than 10 Hz, while the high-cut filter can go as low as 500 Hz, if necessary (Figure 13).

The following non-pathologic subject factors that can alter the evoked response.

(a) **Peripheral nerves** age faster than central nerves. Median nerve conduction slows by approximately 0.16 m/sec/yr, whereas the central-conduction velocity remains stable to age 60, then slows 0.78 m/sec/yr.
(b) **Infants**: SSEP can be recorded at any age. The interpeak latency (IPL) shortens rapidly from age 0–2, and the IPL shortens slowly over the age 2–6. Adult normative values establish at age 8.
(c) **Gender**: The latency of response for females is shorter than those of males by 1 msec in central conduction in SSEPs recording.
(d) **Body size**: Use of Erb's Point as a marker to correct for limb size.
(e) **Body temperature**: In limbs, there is a faster conduction at higher temperatures; the increase follows at a rate of 5 percent per 1 degree centigrade. Therefore room temperature should be kept constant at 21–23 degrees centigrade and skin surface should be maintained at 34 degrees centigrade (37 degrees centigrade core temperature). In the central pathways, there are few, if any effects of temperature changes.
(f) **Sleep, Level of Consciousness**: Both have no effect on median SSEPs.
(g) **Medication, anesthetics**: most cardiovascular drugs do not affect SSEPs. All sedatives such as barbiturates, propofol, and volatile anesthetics as well as opioids affect latency and amplitude height of evoked potentials, an effect which is dose-concentration related. When using ketamine there is an increase in amplitude, which however, is combined with an increase in latency. Similar to phenytoin all antiepileptics slow central conduction velocity in proportion to serum drug levels.

SSEP serve to detect pathology, localize a deficit, and (in a limited way) gauge severity and character in a nerve conduction disorder.

Posterior tibial nerve evoked potentials

The N_{20} peak is generated in the lumbar spine at root entry of cauda equine and is used as a reference point for measurements in conduction velocity. The next P_{37} peak is generated in the primary somatosensory cortex, while the following N_{46}. P_{66}, and N_{74} all originate at higher cortical centers (Figure 14).

The montage for peripheral and central nervous system measurements is a two channel recording where

Channel 1: Lumbar spine L2 – iliac crest (see Figure 44)
Channel 2: Cz′ – Fpz all with grounding at knee

Recommended equipment setting is as follows:

Gain = 10 μV
Sweep = 10
Scale factor = 2
Repetition rate = 2.11–4.22/sec
High-cut filter = 2000 Hz
Low-cut filter = 10 Hz
Averages = 200
Artifact rejection = on

Use the above protocol recommendations and replicate responses two times for each limb and compare responses for consistency. If the waveform is unclear, increase stimulus intensity slightly, and decrease repetition rate. Also, check electrodes and instrument settings. In case of too much

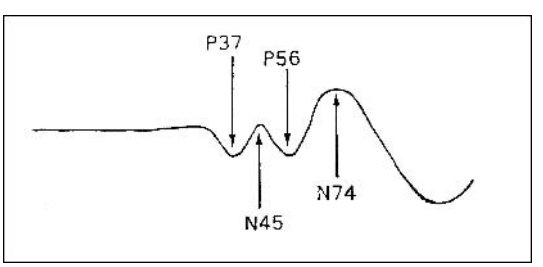


Fig. 14. Early-evoked somatosensory-evoked responses following posterior tibial nerve stimulation.

Table 3. Normative values derived at posterior tibial nerve stimulation

	Wave	Mean (msec)	Std. Dev. (msec)
ABSOLUTE VALUES	L.S.	19.9	1.8
	P37	36.3	2.4
INTERPEAK LATENCIES	L.S.-P37	16.4	1.4
LEFT-RIGHT DIFFERENCES			
	L.S.	0.4	0.3
	P37	0.6	0.4

noise, increase the number of averages, relax the patient and if sedation is required use 10 mg diazepam p.o. at pre-test.

For analysis, check the morphology of waveforms, look for the typical negative/positive deflections. Move cursor to center of peak (this is reference point for following central measurement. Then evaluate the Cz – Fpz waveform and see if the negative wave is in vicinity of 37 msec. Then place the cursor at the peak to judge arrival at cortex comparing the normative values (Table 3).

Factors, which alter the response in event-related posterior tibial nerve stimulation

Non-pathologic stimulus factors that can alter the response.

(a) The mode of stimulation – there is a better response on electrical than tactile stimulation. For example, a tendon tap gives later and smaller response.
(b) The **stimulus intensity**: With higher intensity there is no change in latency. However, amplitude increases as intensity increases until the foot twitches. Do not further increase intensity afterwards.
(c) The **repetition rate**: The amplitude remains constant over the range of 0.5 to 5/sec (Hz). There are no significant latency changes with increased repetition rate. It is possible to get responses to rates as high as 50/sec.
(d) The **filter settings**: Since the response is in the range of 25 to 2500 Hz, the low cut filter should not be higher than 10 Hz, and the high-cut filter can go as low as 500 Hz if necessary.

Non-pathologic subject factors that can alter the response.

(a) **Age** has a similar effect on tibial nerve conduction velocity as on the median nerve, i.e. nerve conduction slows by approximately 0.16 m/sec/yr, whereas the central-conduction velocity remains stable to age 60, and then slows 0.78 m/sec/yr.
(b) **Infants**: The posterior tibial nerve evoked potentials can be recorded at any age. There are only few studies available, which indicate that the peripheral nerves are mature at the age of 3, and the central pathway responses are established by the age of 5.
(c) **Gender**: There are no marked effects aside from smaller limb size in female.
(d) **Body size**: Use of lumbar potential serves as a marker to correct for limb size.
(e) **Body temperature**: In limbs there is a faster conduction at higher temperatures; the increase is by 5 percent per 1 degree centigrade. Therefore room temperature should be kept at 21–23 degrees centigrade, while surface temperature of the skin should be 34 degrees Celsius, which corresponds with 37 degrees centigrade core temperature.
(f) **Sleep, level of consciousness**: Both states do not affect amplitude and latency.
(g) **Medication**: Most cardiovascular drugs do not affect Posterior tibial SSEPs. However, all sedatives such as barbiturates, propofol, and volatile anesthetics as well as opioids affect latency and amplitude height of evoked potentials, an effect which is dose-concentration related. In addition, epidural opioids and/or local anesthetics markedly affect latency and amplitude height. Similar to phenytoin all antiepileptics lower central conduction velocity in proportion to serum drug levels.

Posterior tibial nerve evoked potentials serve to detect the pathology, localize a deficit, and in a limited way, gauge the severity and the character of a disorder depending on generator location (Figure 15).

Summary of parameters for median nerve SSEPs

Stimulus parameters

Stimulus – electrical pulse
Duration – 100 μsec
Rate – 2.11/sec

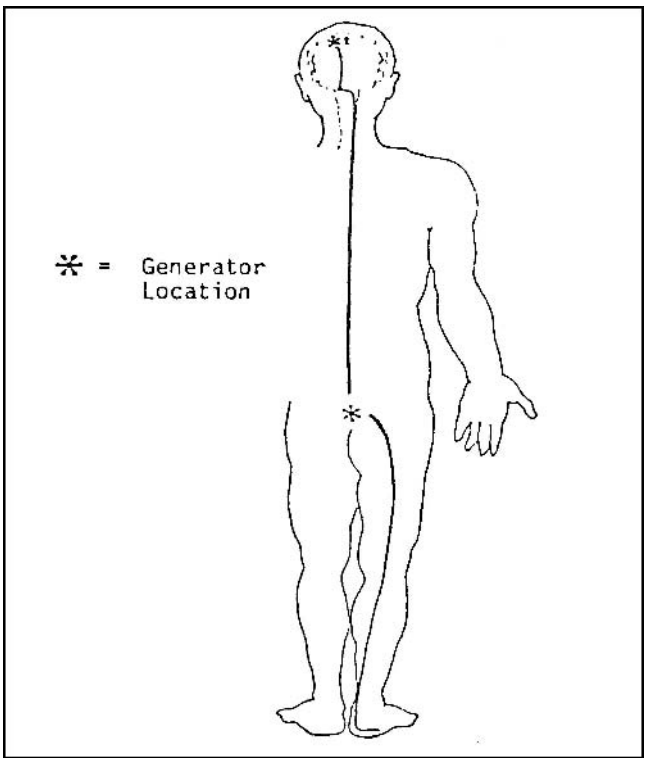


Fig. 15. Generator location where peaks originate in posterior tibial nerve stimulation.

Instrument parameters

Gain – 10 or 20 μV/division
High-cut filter – 500 Hz
Low-cut filter – 10 Hz
Sweep speed – 5 msec/div (50 msec/epoch)
Scale factor – 1 or 2
Averages – 200
Artifact rejection – off

Electrode location for upper extremity (median nerve) stimulation

Reference – Fz
Active – 2 1/2 cm posterior to Cz and 7 cm lateral to midline at Cz′
Ground – on the stimulated shoulder or elbow

Alternative recording sites

Erb's point – Located ipsilateral to the peripheral nerve being stimulated. Place the electrode in the fossa above the clavicle and 1 cm lateral to the border of the sternocleidomastoid muscle. Pressure on that point will produce discomfort.

Cervical VII – This site lies over the spinal pathways. Place the electrode just above the most prominent cervical vertebra (C VII) also known as the vertebra prominent. Have the subject drop his head down. Find the largest protrusion of the vertebra approximately at the upper shoulder level.

Cz′ – This site lies over the primary somatosensory cortex subserving the right-hand region and is located contralateral to the right arm. To find Cz′, measure 2 1/2 cm posterior to Cz along the midline. Next to a line extending from this point to the ear canal contralateral to the stimulation, place the electrode 7 cm from the midline.

Reference site – Fz, the middle of the forehead.

Ground site – Located at the stimulated limb at the elbow.

Sequence of measurement in median evoked potential

1. Apply the electrical stimulus to the median nerve at the wrist at a rate of 2 or 5/sec (2–5 Hz), gradually increasing the intensity, until a motor response (thumb twitch) is observed or the stimulus becomes intolerable. Reduce the intensity just above motor threshold.
2. Collect the replicated evoked responses.
3. Display the waveforms and evaluate them for reproducibility.
4. Identify the prominent peaks. Print out the waveforms.
5. Measurement of nerve conduction velocities. Measure the arm length with the arm extended to a rectangular position (90°) at the shoulder. Measure from negative peak at Erbs's point (peripheral component) to the peak derived at the electrode at position C VII vertebra.
6. Calculate the nerve conduction velocity at the extremity using the following formula

$$\text{Conduction velocity} = \frac{\text{Arm length (cm)} \times 100}{\text{Latency of Erb's point potential}}$$

7. Compare the responses in short and tall individuals.
8. Calculate the central conduction time using peak N_{10} at CII vertebra to N_{20} (cortical component) derived from the scalp electrode.

Summary of parameters for posterior tibial nerve SSEPs

Stimulus parameters

Stimulus – electrical pulse
Duration – 100 μsec
Rate – 2–5/sec

Instrument parameters

Gain – 10 or 20 μV/division
High-cut filter – 500 Hz

Low-cut filter – 10 Hz
Sweep speed – 10 msec/div (100 msec/epoch)
Scale factor – 1 or 2
Averages – 200
Artifact rejection – off

Electrode location for upper extremity (median nerve) stimulation

Reference – Fz
Active – Cz′, which is located 2 1/2 cm posterior to the vertex along the middle line
Ground – on the stimulated leg or the knee

Sequence of measurement in tibialis posterior nerve evoked potentials

1. Apply the electrical stimulus to the distal part of the posterior tibial nerve at the ankle at a rate of 2 or 5/sec (2–5 Hz) and an intensity just above motor threshold. By gradually increasing the intensity the motor response (downward flection of the toes) is observed or the stimulus becomes intolerable. The posterior tibial nerve is located on the medial aspect of the ankle behind the medial malleolus.
2. Collect the replicated evoked responses such as the N_{20} at the lumbar spine and the P_{37}, N_{46}, P_{56} and N_{74} derived at the primary somatosensory cortex, which reflects the response at the higher cortical centers.
3. Display the waveforms and evaluate them for reproducibility.
4. Identify the prominent peaks. Print out the waveforms.

REASONS TO MONITOR EVOKED POTENTIALS

Sensory evoked potentials present a neurophysiologic procedure performed to guarantee the integrity of both cranial and peripheral nerves during surgery. The procedure monitors nerve function by activating or stimulating a nerve or group of nerves primarily to observe the contractions of the muscle groups affected by the stimulation of a nerve or particular group of nerves. Intraoperative monitoring of somatosensory evoked potentials (SSEPs) is used during orthopedic or neurologic surgical procedures to reduce surgically induced morbidity and/or to monitor the level of anesthesia. SEP are electrical waves that are generated by the response of sensory neurons to stimuli. Changes in the electrical waves are averaged by a computer and then interpreted by a physician. The SSEPs can then be used to assist the diagnosis of certain neuropathologic states or to provide information for treatment management.

A. Intraoperative neurophysiological monitoring may be cost shared during surgical procedures that could potentially cause harm to the brain, spinal cord or peripheral nerves. Visual, auditory, and somatosensory evoked potential recordings are considered eligible for coverage for the following indications:

1. Visual evoked potentials.

   (a) To diagnose and monitor the acute and chronic phase of multiple sclerosis.
   (b) To localize visual field defects occurring in the absence of structural lesions, acquired metabolic disease or infectious disease.

2. Auditory evoked potentials.

   (a) To evaluate brainstem function and metabolic disorders;
   (b) To identify the presence of brainstem tumor when MRI or CT is ineffective or unavailable;
   (c) To diagnose and monitor demyelinating or degenerative brainstem diseases, such as multiple sclerosis, central pontine myelinolysis and olivopontocerebellar degeneration;
   (d) To diagnose the presence of lesions in the external auditory system, such as acoustic neuromas;
   (e) To assess recovery brainstem function after removal of space occupying lesions compressing the brain stem;
   (f) To supplement of the EEG in evaluating brain death or irreversibility of coma; and
   (g) To measure the type and extent of hearing impairment or determine the degree of neural maturation in neonates, infants, and children less than five years of age.

3. Somatosensory evoked potentials.

   (a) To assess somatosensory function in unconscious patients who have sustained traumatic damage to the spinal cord which is demonstrated by radiologic examination and who are candidates for emergency surgery of the spinal column,
   (b) To diagnose and manage suspected space occupying lesions or demyelinating and degenerative diseases in the somatosensory system not identified by radiologic examination,
   (c) To monitor large tumors which may cause significant brainstem compression or ischemia (deficiency of blood supply),
   (d) As an indicator during operations when surgical intervention/manipulation puts the spinal cord at

risk (e.g., sclerosis surgery, resection of spinal arteriovenous malformations, removal of intraspinous tumors and some cervical discectomies),
(e) To monitor surgery during intracranial aneurysms; and lastly.
(f) To monitor a sufficient depth of analgesia.

Contrary, electromyography (EMG) is used in following situations:

1. To monitor cranial nerves, with recording from muscles innervated by nerves which are in jeopardy during surgery for removal of tumors of the skull base (e.g., acoustic neuromas, neuromas of other cranial nerves, meningiomas, glomus jugular tumors);
2. To monitor muscles innervated by specific peripheral nerves during surgery that poses risks to nerves and/or spinal roots (e.g., removal of lumbrosacral tumors or other lesions in the region of the cauda equina, tumors of the brachial or lumbar plexus, repair of peripheral nerve lesions); and
3. To monitor facial nerves as extracranial procedures (e.g., removal of tumors of the parotid gland).

As previously stated the electroencephalogram (EEG) and the compressed spectral array (CSA) of the EEG may be cost shared to monitor for carotid endarterectomy and brain surgeries that could potentially compromise cerebral blood flow. Therefore policy considerations for reimbursement of intraoperative neurophysiology testing is limited to the DRG amount, when billed by an authorized institutional provider, or may be reimbursed separately from the global surgical fee when billed by an authorized professional provider, including the physician performing the surgery. In addition, there is are exclusions for reimbursement:

1. For simple laminectomies or other spinal procedures, which do not entail significant risk to the spinal cord.
2. For monitoring of the sciatic nerve during total hip replacement.
3. To assess the status of the somatosensory system in unconscious head injury patients.
4. To define conceptional or gestational age in pre-term infants.

BASIC PRINCIPLES OF EVOKED POTENTIALS – WHAT IS AN EVOKED POTENTIAL?

An evoked potential is an electrical by-product of activity in peripheral and central neural pathways in response to an external stimulus (Figure 16). The advantages of recording evoked potentials are:

Fig. 16. With the introduction of evoked potentials, the run through the mill clinician faces a completely new method, not knowing how to benefit from it.

(a) To obtain functional information about specific neuronal structures,
(b) An objective measurement in nerve activity,
(c) To use a non-invasive technique,
(d) To use a rapid and yet simple procedure.

Basic consideration when using sensory evoked potentials for monitoring

The evoked potential is useful for:

(a) Demonstrating normal nerve function,
(b) Detecting abnormal nerve function,
(c) Localizing a problem to a segment of the conductive pathway of,
(d) Characterizing the severity of a problem.

On the other hand, the evoked potential is not useful for:

(a) Giving psychophysical information from higher centers in the brain.
(b) Giving absolute normal/abnormal answers, since the results are statistical derivations.

(c) Characterizing the origin of pathology that is causing an abnormal response.

Evoked potential show the following characteristics and definitions:

(a) An evoked potential has a low amplitude (0.1–20 μV).
(b) There are evoked potentials with short latency, which generally is less than 100 msec.
(c) There are evoked potentials with long latency, which generally is more than 200 msec.
(d) The evoked potential is usually buried in noise, which originates from both outside the body (exogenous noise) and inside (endogenous noise).
(e) In order to derive an evoked potential it is necessary to optimize the signal to noise ratio.

The signal during evoked potential recording is defined as nerve activity associated with reception, transmission, and processing of a stimulus. Nerve activity is electrical activity, which is picked up at the scalp and relates directly to processes in nerve cells and fiber tracts. Several factors have to be considered in moving from activity in neural "generators" to scalp fields:

1. The activity in nerve fibers–membrane events.
2. Local electric field characteristics.
3. Transmission of currents from the cortex to the scalp through fluid, skull and skin.

Nerves have electrical fields, which are associated with them.

(a) This is because charged ions are actively moved across the nerve membrane to create a potential difference between the interior and exterior of the axon with a potential of <75 mV neg. inside. When an action potential is generated, the potential briskly, locally reverses.
(b) Regions of positive and negative charges are separated along the surface of the neuron (generator), and a transient electrical field is set up with the following equation obeying Coulombs law: $E = Q \times R^2$.
(c) At the stimulation site field strength is proportionate to the amount of charge.
(d) Field strength is inversely proportional to square of distance from charges, and
(e) Transient current flows between separated charges.

At the cortical surface, electrical field intensity and gradient are determined by distance and orientation of the source, from which near-field and far-field potentials can be recorded.

(a) The near-field potential is characterized by a small spread and a steep gradient, while
(b) The far-field potential is characterized by a wide spread and shallow gradient.

An evoked potential has to pass through cerebrospinal fluid, and membranes covering the brain, the bony skull, and the skin all of which diffuses the potential, causing a decrease in amplitude and a blurred spatial distribution, which makes it necessary to eliminate all other electrical noise from around the patient.

One can reverse the chain, projecting back from scalp activity to the neural generator. This, however, is complicated by a number of factors:

(a) Fields from different generators overlap, adding in time and space, making individual contributions difficult or impossible to distinguish.
(b) There are open and closed fields: For reasons of fiber length, synchronicity, and geometry not all nerve activity generates external fields. In addition, what we know about human brain is not enough. Animal models offer only limited help and it is still debated whether axons or dendrites act as primary generator.
(c) The cortex is convoluted: Generators have different orientations, sizes, and time courses of activity in different individuals. Often, one can only approximate generator location. But, that's enough because the brain is small. For example, the question if the brain stem evoked potential (BSEP) wave V generator is in the lateral lemniscal or inferior colliculus is of less importance, since these anatomical features are physically less than 1 cm apart, an insignificant distance from the clinical viewpoint.

Contrary to evoked potentials, the EEG presents the electrical activity from only a small portion of the cortex. Furthermore, the varying changes of different anesthetic agents and the different depths of anesthesia can be monitored. Aside from using the spectral edge, more sensitive methods can be used to fully understand the way in which anesthetics act on the brain, and more so, how function is impaired. There are different modalities in evoked potential recording, being either the Acoustic Evoked Potential (AEP) tracing, the somato-sensory-Evoked Potential (SSEP) tracing or the Visual Evoked Potential (VEP) tracing.

The principle of the evoked potential is to apply a stimulus and then to record the electrical change of the signal along its specific pathway up to the corresponding region of the brain. The stimulus may be of either visual, auditory or of somatic nature.

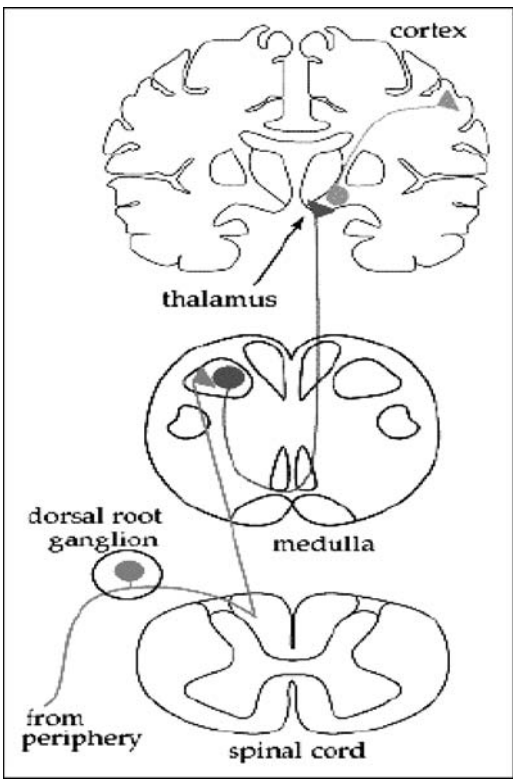


Fig. 17. Principle of the pathway of the somatosensory stimulus, which can be recorded along the sensory tract.

In case of somatosensory evoked potential measurement (Figure 17) the stimulus is a small electrical potential applied to the skin of the hand or the foot. Thereafter, the stimulus travels along the specific nervous pathways inducing (= generating) potential activation at various sites. The generation of potential changes at various sites along the pathway is an index for the integrity of the nerve. Thus, the evoked potential can be considered a neurophysiological response (usually of the cortex) to impulses originating from some externally stimulated sensory nerve. They provide a physiological measure of the functional integrity of the sensory nerve pathway, which can be used as a clinical diagnostic tool as well as for intraoperative monitoring. The evoked potential usually is recorded from the specific cortical area corresponding to the stimulus input. For instance the stimulation of sensory nerves will result in impulses traveling along the peripheral nerve, the spinal cord and finally ending at the contralateral, post-Rolandic sensory cortex (Figure 17).

An evoked potential differs from the EEG mainly in two ways:

1. The EEG is a random, continuous signal, which arises from the ongoing activity of the outer layers of the cortex. An evoked potential is the brain's response to a repetitive stimulus along a specific nerve pathway.
2. EEG signals range from 10–200 milliVolt (mV). Evoked potentials are smaller in amplitude (1–5–20 μVolt) requiring precise electrode positioning and special techniques (signal averaging) to extract the specific response from the underlying EEG 'noise'. The technique of signal averaging, as originally described by Dawson in 1954 [3], has been further developed in computer processing. The technique is now used by applying a stimulus repeatedly – preferably at randomized intervals – and to record the evoked response over the corresponding area of the brain, averaging out mathematically the change over the number of stimuli.

RATIONALE FOR THE USE OF EPS IN THE OR AND THE ICU

Evoked potentials (EPs) serve the following major purposes:

1. Monitoring of the functional integrity of neural structures that may be at risk during, for instance, ECC (extracorporeal circulation) or endarterectomy indicating cerebral hypoxia.
2. Monitoring of the effects of anesthetic agents and other centrally active drugs, which, besides the cortex, affect deeper neuronal structures.
3. Orthopedic cases where the spinal cord is at risk such as Harrington rod insertion and removal.
4. Clamping of the abdominal aortic artery during aneurysmectomy resulting in a potential damage of the lower parts of the spinal cord.
5. Clipping of an intracerebral aneurysm, which may be impeding blood flow to vital cerebral textures.
6. An indicator of cerebral hypoxia when the blood pressure is deliberately lowered.
7. Operation on peripheral nerves and nerve roots to identify early trauma.
8. Monitoring the cerebral function during controlled hypothermia when the EEG becomes flat.
9. Monitoring of pathophysiological conditions following severe head trauma and the effects of therapy.
10. An intraoperative warning device of insufficient analgesia during light anesthesia when movement is abolished by muscle relaxants and cardiovascular responses are modified by vasoactive drugs.

The classification of evoked potentials

Stimulating a sensory nervous pathway induces evoked potentials. If the auditory nerve is stimulated by 'clicks' from headphones, it is called the auditory evoked potential

(AEP). The early part of the AEP waveform (less than 10 msec) is called the Brainstem Auditory Evoked Potential (BAEP) since it reflects the passing of the impulse through the brainstem.

If a small electrical current applied to the overlying skin stimulates a nerve on the arm or the leg, it is called the Somato-Sensory Evoked Potential (SSEP). If, however, the retina is stimulated by means of flicker light or a sudden change in a checkboard pattern, the evoked potential thus recorded over the corresponding cortical area is called the Visual Evoked Potential (VEP). Evoked potentials are used both as a diagnostic tool and as a monitoring technique. As diagnostic tests, evoked potentials are useful to evaluate neurologic disorders such as:

(a) Multiple sclerosis,
(b) Acoustic nerve tumors, and
(c) Optic neuritis.

As a monitoring modality, evoked potentials are used during all surgical procedures, which might compromise part of the brain or the spinal cord.

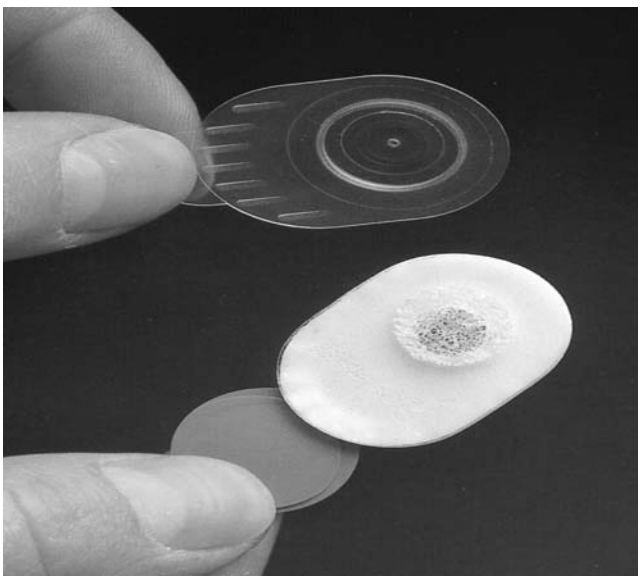


Fig. 18. A pregelled self-adhering pad electrode type for the stimulation of peripheral nerves.

The principle of somato-sensory evoked potential (SSEP) monitoring

There are distinct differences between the recording of evoked potentials and the recording of an EEG for spectral analysis:

(a) The electrode must be placed on specific locations on the scalp necessitating the use of conventional cup or needle electrodes and not ECG pad electrodes.
(b) The evoked potential waveform is produced by repeatedly averaging segments of the EEG following a sensory stimulus. Thus, a specific and repetitive stimulus must be provided and there will be a lag of up to several minutes before the results of the test are known.

Type of electrode for stimulation and recording of SSEPs

In recording SSEPs two sets of electrodes are used. One is for detecting and for recording the impulse, while the other set is for providing the electrical stimulus to the nerve. For stimulation, regular self-adhesive ECG electrodes can be used or a dual pregelled and self-adhering PNS (peripheral nervous surface) electrode is recommended (Figure 18).

Localizing the exact stimulus site for SSEP recording

1. A bar stimulator cable that comes with every device, intended for the measurement of SSEPs is plugged into the stimulator.
2. With the patient's hand palm-up, a neutral relaxed position is obtained. Relaxation is important for obtaining good SSEPs.
3. The inner surface of the wrist is wiped with alcohol to remove skin oils.
4. The area then has to be dried completely, as otherwise alcohol will break down conductive gel.
5. A small amount of conductive gel is placed on each disk of the bar electrode.
6. Location of the nerve to be stimulated:

   – Median Nerve. Lateral to the tendon that runs down to the wrist towards the thumb (Figure 19).
   – Posterior tibial nerve; the inside of the ankle between the medial malleolus and the Achilles tendon.

7. The stimulating bar is placed over the median or posterior tibial nerve, cathode proximal (Figure 19).
8. Explain to the patient that he or she is going to feel some pulses at the wrist or ankle, which will begin at low level and increase until the thumb or the toe twitches.
9. A toggle at the stimulator box is depressed to the 1 sec position.
10. Thereafter the intensity knob for current is turned on and increased slowly until the patient can feel the pulse. For median nerve the patient should feel the pulse travel down towards thumb and index finger.

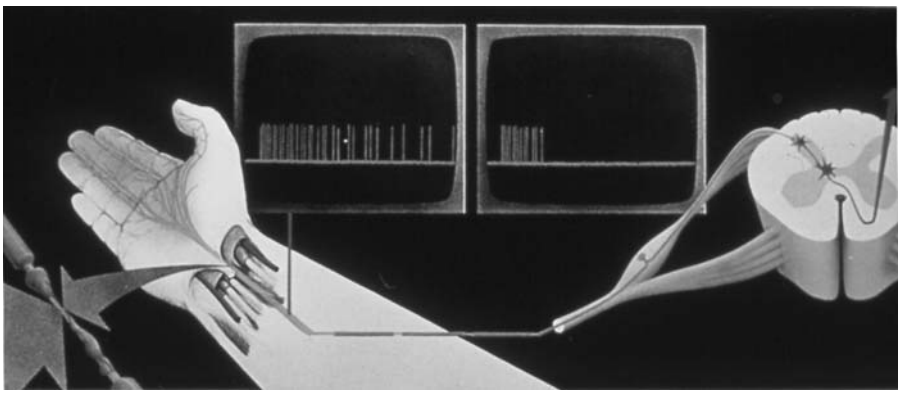


Fig. 19. Localization of the median nerve which is stimulated and from where ascending volleys travel up the sensory pathway via the dorsal root of the spinal cord.

The pulse should not be felt in the little finger, as this is the ulnar nerve. For posterior tibial nerve stimulation the pulse should travel down to the sole of the foot to the big toe. If the pulse is felt over the heel, stimulation is over the wrong branch of nerves. Change the location of the bar stimulator. A light at the stimulator box will flash each time a pulse is delivered.

11. If necessary, the stimulating bar has to be moved in order to find the optimum stimulus location. Sometimes pressure on the bar has to be applied, as the nerve is located deep below the skin. Avoid gel from one electrode to connect with the other. This would result in a 'bridge' and shorts out the stimulus.
12. Once a pulse is felt in the correct location and thumb or toe twitches, the stimulus intensity on display should be remembered for later stimulation recording. The toggle switch on the stimulator is switched back to the center position.
13. The stimulating area is now cleaned with alcohol and dried completely.
14. Pre-gelled pediatric ECG disc electrodes are applied to the exact location of the bar electrodes and connected with the stimulator cable.
15. The stimulation electrodes, the cathode, or the negative pole (red), and the anode, or the positive pole (black), are placed 2–3 cm apart (Figure 20).

As the current flows from the anode to the cathode, a negative charge is accumulated at the cathode near the nerve surface resulting in depolarization (Figure 21). The positive charge accumulated at the anode near nerve surface leads to hyperpolarization.

Stimulus intensity necessary for median evoked potential

The stimulus, which is necessary for initiating an event, is of a square wave nature, has a preset duration, amplitude and repetition rate. In SSEP recording the following parameters are selected for stimulation:

(a) A duration of up to 100 ms,
(b) An amplitude of 5–10 Volt constant current resulting in 5–30 mA, and
(c) A repetition rate between 5–10 Hz.

A visible and maximal motor twitch has to be elicited, which has the following classifications:

(a) Subthreshold – no axons fire
(b) Threshold – some axons fire
(c) Sub-maximal – more axons fire
(d) Supra-maximal – all axons fire.

Voltage and current necessary for each individual may vary greatly. Sub-maximal motor stimulation is usually enough to fire all of the sensory axons. The most important consideration for adequate stimulation is the stimulation over a large nerve and the eliciting of motor responses. The information, therefore, is complex with inputs reaching the central structures at different times [4].

In order to reduce stimulation artifacts, which may jolt the preamplifier input, the following facts have to be taken into consideration:

(a) Isolate the stimulus from the recording electrodes with a separate transformer,
(b) Keep the stimulator away from the recording electrodes,
(c) Remove perspiration from the stimulating area,

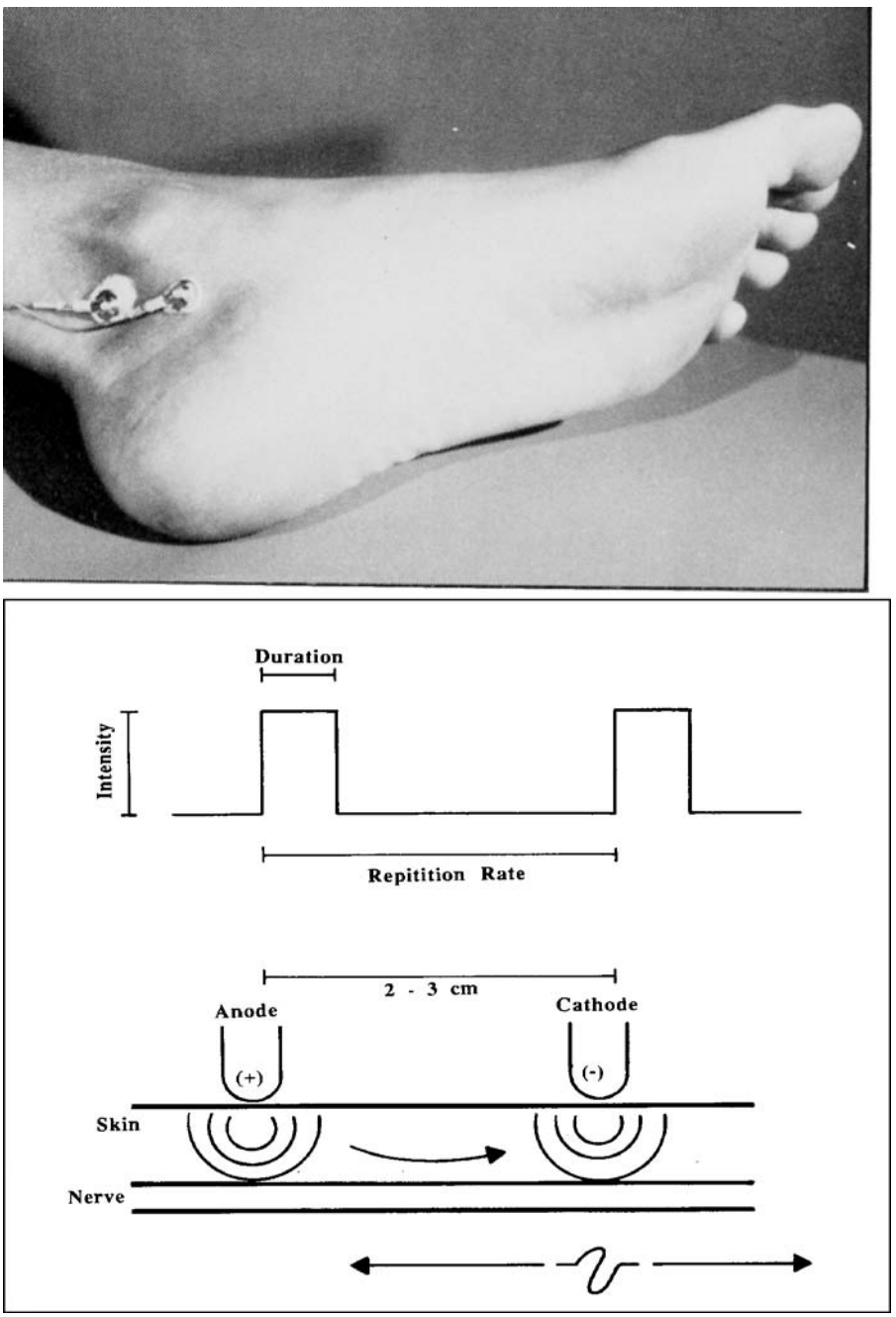


Fig. 20. Representative tibialis posterior stimulation, where the cathode (similar as in median nerve stimulation) has to be placed close to the recording site as not to diminish the amplitude of nerve volleys that travel along the nerve pathways.

(d) Keep recording and stimulating electrode impedance low,
(e) Keep the recording leads away from the stimulator as they work like antennas,
(f) Place a ground between stimulator and the recording electrodes.

From the point of origin, the stimulation site, volleys of impulses travel along the peripheral nerves, the nerve plexus, and enter the dorsal column of the spinal cord. From there the ascending lemniscal pathways take the stimuli to the thalamus and the primary sensory cortex (Figure 22) [6]. The ascending volley can be

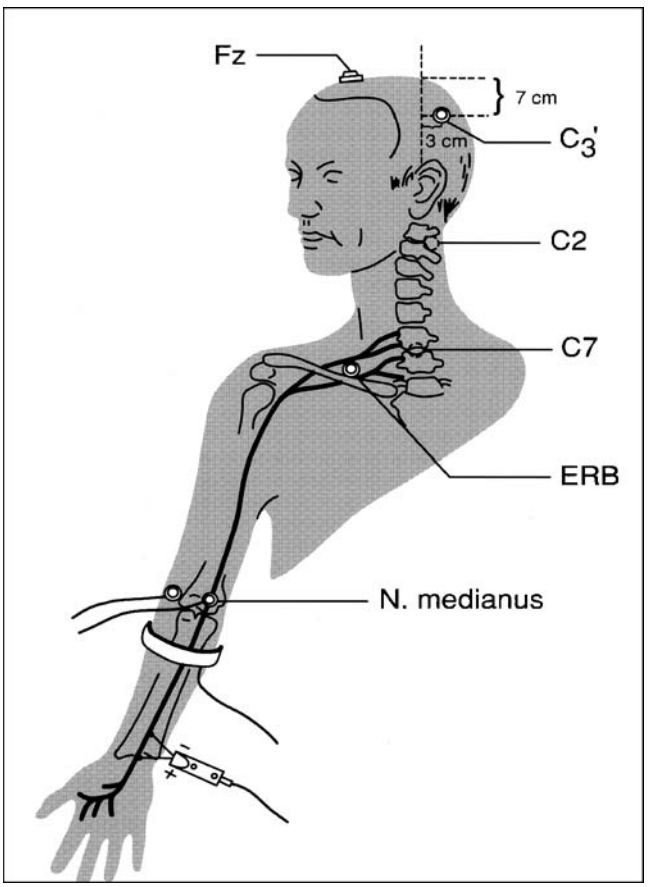


Fig. 21. The two prongs at the stimulation site for median evoked potential recording, where the cathode is located proximally in and the ground (Velcro strap) between stimulation and recording site. Various points along the sensory pathway are used for recording of evoked potentials and evaluation of integrity.

recorded from any of the several sites along this pathway [7].

The recording electrodes

The recording of the SSEP is done with a pair of electrodes. One of the electrodes is placed over the anatomical site, which corresponds to the location along the sensory nerve pathway, which is most likely to detect an impulse. This is called the active site. The other electrode is placed in a location not involved in the pathway response. This is called the referential site. As electrodes are placed on specific scalp locations to obtain a maximum response to a sensory stimulus, the international 10/20-system measurement, the standard of neurological practice, is used.

Measurements are made using bony landmarks on the skull as reference points. With this technique it is possible to consider interindividual differences in circumference and shape of the skull and find the location on the skull, which is above the corresponding area of the stimulated part of the body (Figure 23).

Head measurements to determine electrode location

1. Locate the nasion and the inion. The nasion is the bony ridge between the eyes. The inion is the bony ridge at the back of the head.
2. Measure the distance in cm between the nasion and the inion over the top of the head.
3. Mark with a grease pencil 50% of the nasion-inion distance (= Cz′ the vertex) and 2 cm behind the vertex (Cz′) (Figure 29). Markings are perpendicular to the tape.
4. Locate the pre-auricular points. The pre-auricular points are on each side of the head immediately in front of the ear channel.
5. Measure the distance between the pre-auricular points going through the vertex mark.
6. Mark 50% of the pre-auricular distance perpendicular to the tape crossing the vertex mark Cz. Leaving the tape in place on either side of the vertex mark (Cz), measure down 20% of the total preauricular distance.
7. Make a mark both perpendicular and parallel to the tape. These marks are called C_3 on the left and C_4 on the right-hand side.
8. Measure 2 cm behind C_3 and C_4 at the same level. These marks are called C_3' and C_4' on the left and right-hand side respectively (Figures 25 and 27).
9. The other electrode site on the scalp is the middle of the forehead. This point is called FpZ. Measuring is not necessary since it is the reference and exact location is not critical.
10. There are now 4 electrode locations (FpZ, Cz′, C_3', C_4') on the scalp for recording of SSEP cortical potentials. They are used in various combinations depending on the nerve being stimulated (Figure 26). The list below will show which electrode location will be used for the specific nerve stimulation.
11. An additional electrode may be placed on Erbs point (EP) bilaterally for median nerve stimulation (midpoint of the supraclavicular area = plexus brachialis) or over the popliteal fossa (PF) bilaterally in posterior tibial nerve stimulation (Figure 26). Erbs point is located just above the clavicle and medial to the point of attachment of the sternocleidomastoid muscle (see also Figure 21). The popliteal fossa is located on the back of the leg at the bend of the knee. The electrodes are placed at the popliteal fossa (PF) with the reference 2 cm below.

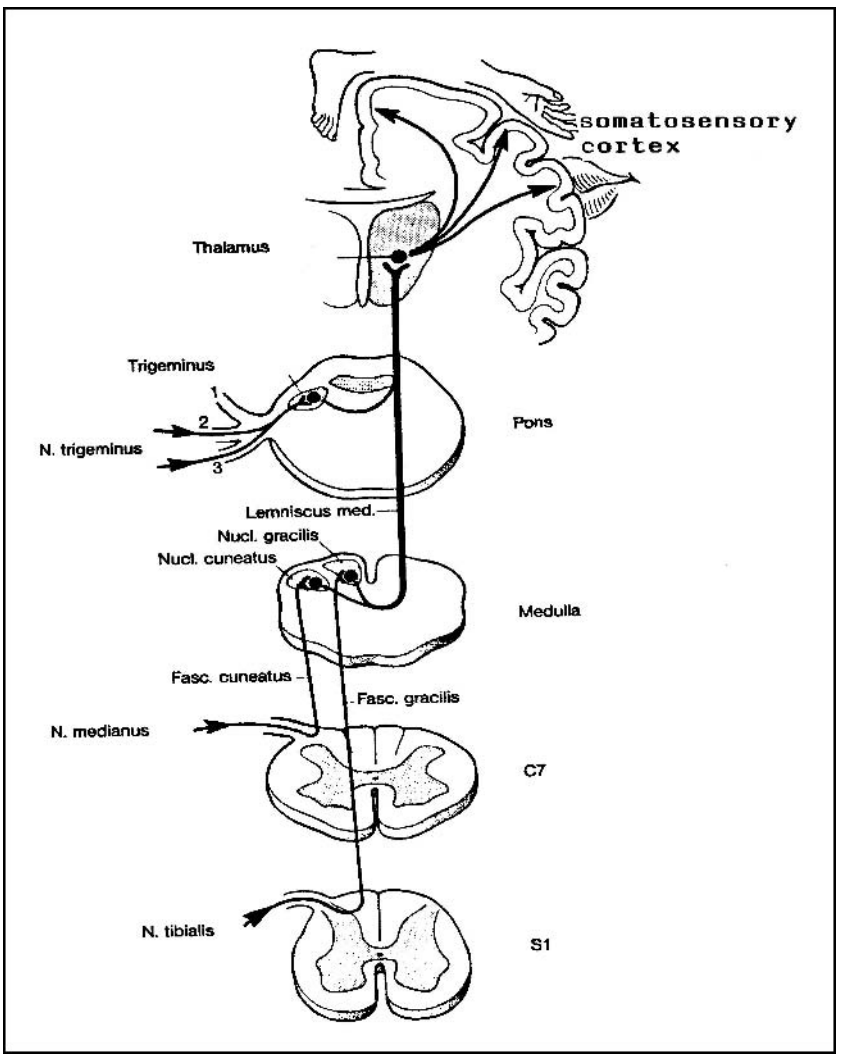


Fig. 22. Pathway of sensory information from the skin to the cerebral cortex. Adapted from [5].

12. A further electrode placement may be used when it is necessary to evaluate the functional integrity of a signal in the spinal cord, using the C7 and C2 locations above the proc. spinosi of the 2nd and 7th cervical vertebra (Figure 21). In posterior tibial nerve stimulation the proc. spinosi of lumbar vertebra can also be used for electrode placement when one wants to check the integrity of the lower sensory nerve and the nerve plexus (Figure 28).

Appliances for electrode placement and removal

The following is a list of materials necessary for the application and removal of the cup electrodes using collodion glue.

1. For measuring the head: a) a tape measure with centimeter markings, and b) a grease pencil.
2. For the application of recording electrodes

   (a) cup electrodes (Ag/AgCl, gold) or needle type (platinum, stainless steel) electrode. The cup electrodes have a doomed top with a small hole in the centre suitable for the application of electrode gel. A highly flexible PVC covered cable is attached to the electrode by a crimp connection. Shrink sleeving covers the joint,
   (b) Collodion,
   (c) Alcohol and acetone prep pads,
   (d) A 5 cc syringe with a blunt tip stub adaptor filled with conductive gel, and optional

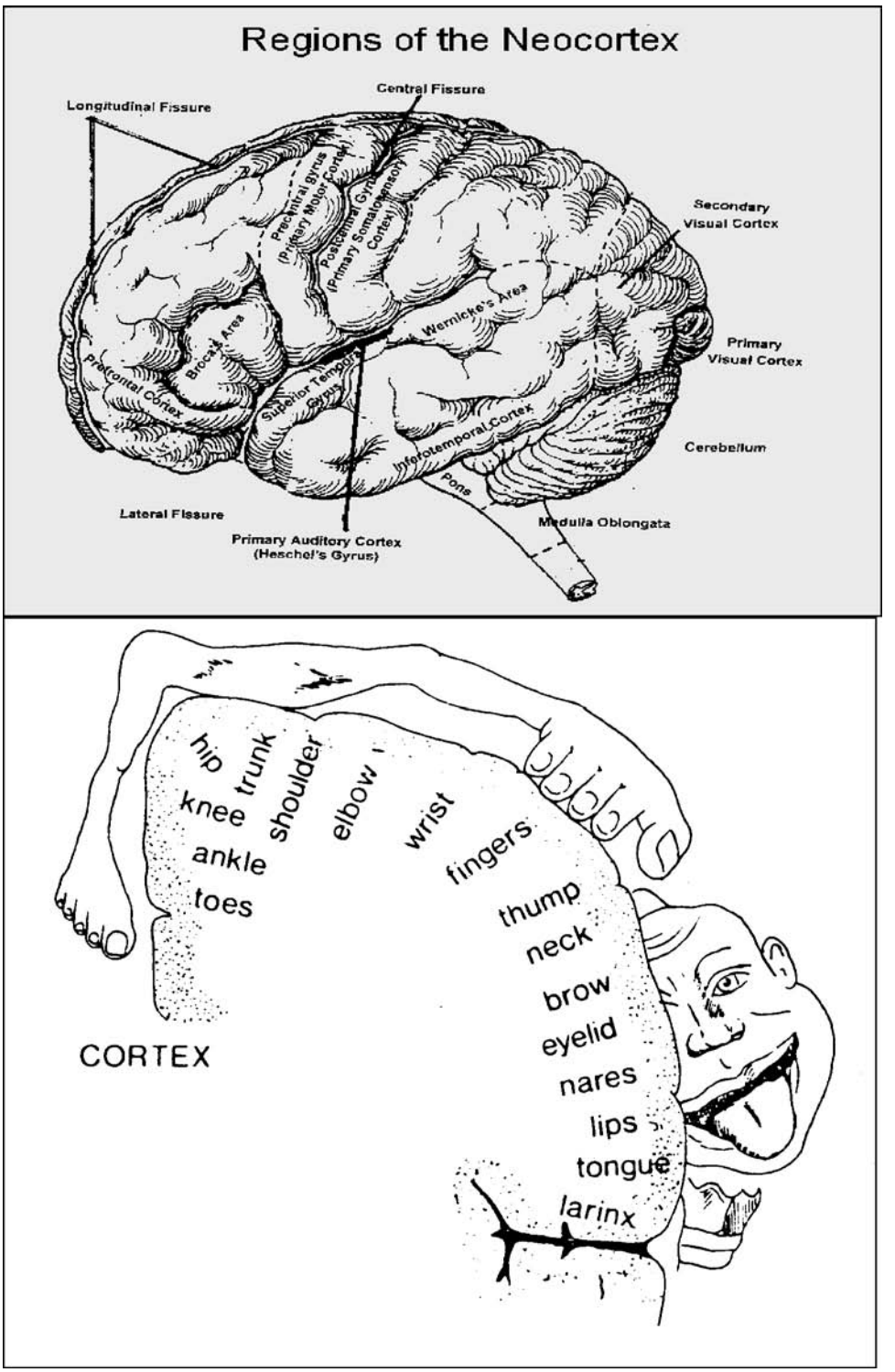


Fig. 23. Localization of the site of input of somatosensory evoked potentials to the primary sensory cortex.

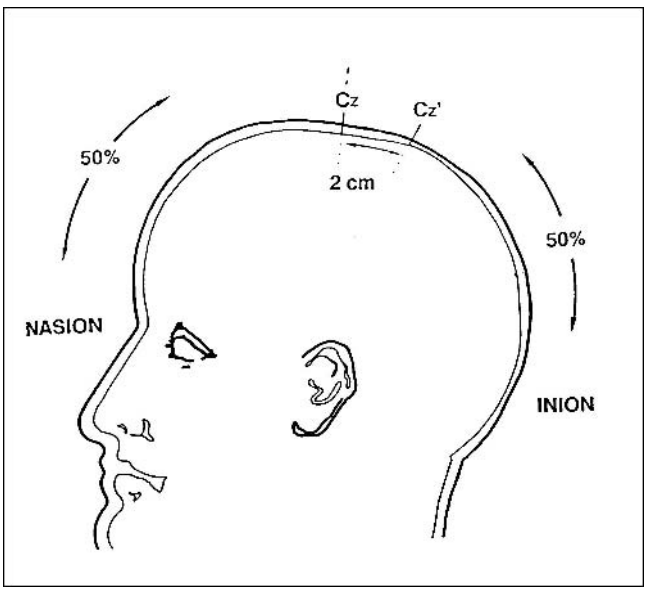


Fig. 24. Localization of the Vertex (Cz) and the Cz′ point, necessary in recording posterior tibial nerve stimulation.

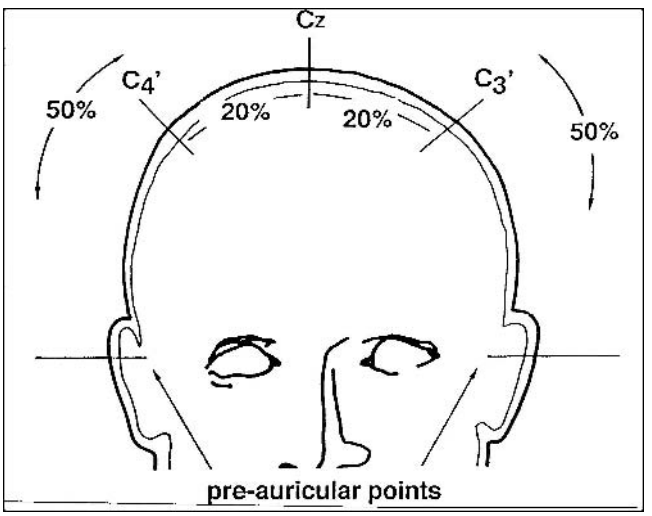


Fig. 25. Procedure to determine C3′ and C4′ respectively for positioning of the active, recording electrode on the scalp overlying the sensory cortex during median nerve stimulation.

(e) An air compressor including hose and applicator tip. This item is designed as an electrode-positioning instrument, an air gun, and as a collodion tube piercer and storage unit. The applicator is provided with a spigot, which fits into the hole of the electrode (Figure 29).

3. For the application of stimulation electrodes:

(a) Bar stimulator to locate site,
(b) Ag/ACL ECG mini electrodes,
(c) Ground plate and strap, and
(d) Conductive gel.

4. Items for removing the electrodes:

(a) Acetone, necessary to remove collodion,
(b) Cotton balls, and
(c) Gauze squares.

When monitoring in surgical situations, it is advisable to monitor two anatomical sites along the nerve pathway at risk. In one channel the active electrode site is over a peripheral nerve such as Erbs Point in median nerve stimulation or the popliteal fossa in posterior tibial nerve stimulation. In the other channel, the active electrode is placed over the sensory cortex site, which corresponds to the nerve being stimulated (Figure 27). Generally, the peripheral nerve response serves as a control. If, for example, only the cortical response is lost it is likely due to the surgical procedure. If both responses are lost it is most likely due to improper stimulation. The inactive electrode is placed on a point that is minimally involved in the sensory pathway. No electrode site on the body, however, will be entirely inactive. Locations, which may be used for the inactive electrode, include the forehead (FpZ), the mastoid, the chin, the shoulder, or a leg.

A Velcro strap electrode is used as a common or ground reference (Figure 30). This electrode is usually placed around the limb being stimulated, between the stimulation site and the first recording electrode. The ground electrode is necessary to improve the ability of the amplifier to reject noise. Its main purpose is:

(a) To maintain a low impedance level, and
(b) To be located near the stimulation site.

As the recording electrodes pick up the evoked response, they in turn are connected to the differential preamplifier. After all noise is filtered out, the sample is converted into digital form and averaged together with other samples. Finally, the computerized information is presented on display. This entire sequence occurs within microseconds.

Similarly, as during power spectral analysis of the EEG, it has to be emphasized, that the electrodes are fundamental to collect a clear evoked response. This is because tiny currents of the evoked potential must be picked up in order to flow through the electrodes. Currents will only flow through electrodes to the extent that this path offers less resistance than the skin path. Therefore, the aim is to minimize as much as possible electrode impedance at the

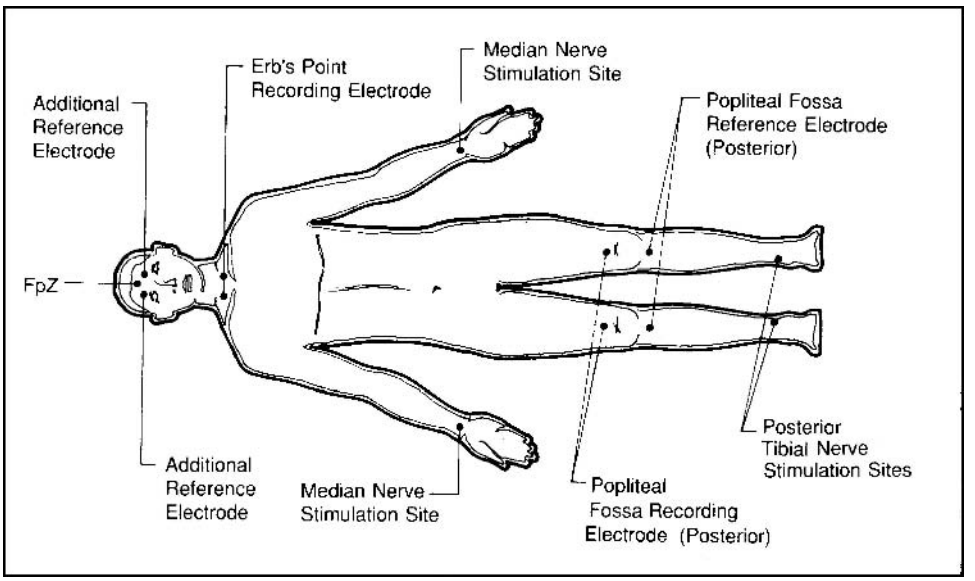
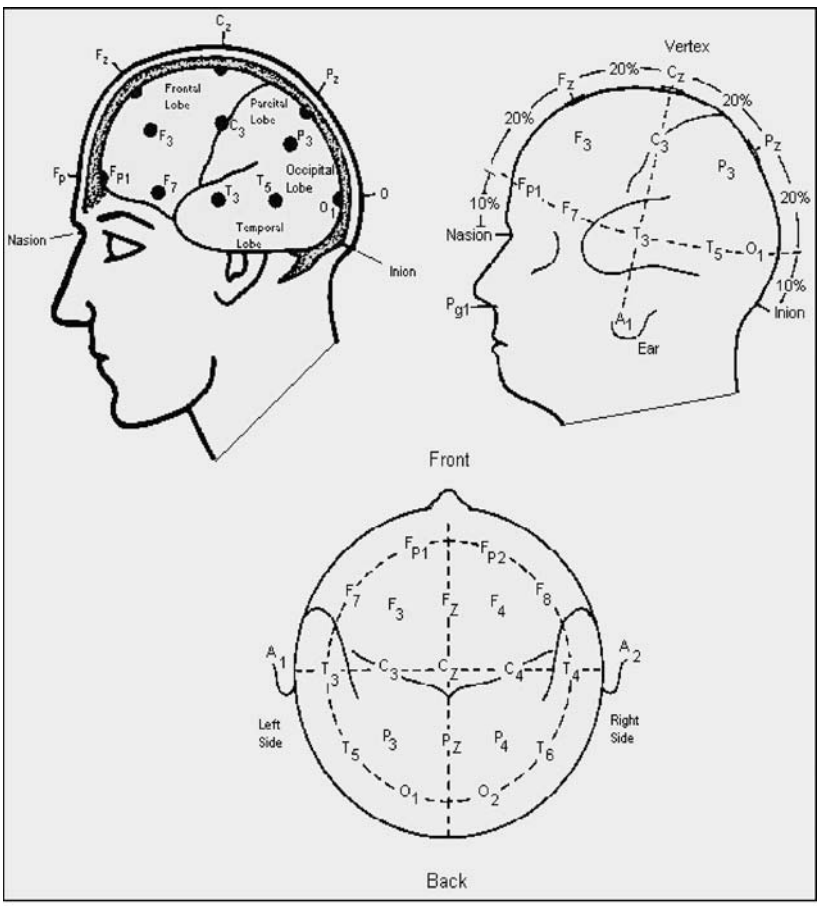


Fig. 26. Common recording sites at median and tibial nerve stimulation. FpZ-reference for right or left median nerve stimulation; C'_3 – for right median nerve stimulation; C'_4 – for left median nerve stimulation; Cz′ – for right or left leg stimulation; FpZ – reference during left or right wrist/leg stimulation.

electrode connection to the skin. This can be achieved by observing meticulously each of the following steps:

1. Part the hair at the recording site.
2. Remove the overlying dead skin (stratum corneum) from the recording site by abrading it with 'Omniprep™' in a circular motion.
3. Remove perspiration and oil (as this spreads the potential, decreases amplitude and increases artifacts) by gently brushing with alcohol.
4. Let recording site dry completely, then tape the electrode firmly to the skin surface with the electrode wire orientated towards the back of the head (Figure 29).
5. Place the tip of the electrode applicator through the hole in the electrode cap to hold the electrode in place and prevent collodion from getting under the electrode.
6. Squeeze a moderate amount of collodion glue around the flange of the cup electrodes and spread it over the entire surface and the adjacent skin.
7. Dry collodion thoroughly using compressed air. After the collodion has been applied around the electrode, blow air from the applicator tap around the flange of the electrode, rapidly drying the collodion and fixing the electrode to the scalp.
8. The cup of the electrode must now be filled with conductive gel using a clean, blunt-tipped specially fashioned needlepoint causing the scalp to be abraded whilst applying the electrode jelly through the hole of the electrode. The skin is being abraded lightly by rubbing back and forth.
9. The ground electrode should next be applied around the arm between the wrist (the stimulation site) and the elbow for median nerve stimulation, or around the leg between the ankle (the stimulation site) and the knee for posterior tibial nerve stimulation (Figures 30 and 31). If both nerves are stimulated, the arm may be used for grounding.
10. Before applying the ground electrode, the area should be thoroughly wiped with alcohol to remove oil. Thereafter, the site should be dried completely with a dry gauze pad.

Conductive gel for the metal ground plate, or physiologic saline solution are applied to the electrode, which is secured around the limb with a Velcro strap, making sure that the cable emerges from the electrode towards the head. Subdermal needle electrodes may also be used for recording. However, different types of electrodes should never be mixed in order to avoid DC potentials. The main reason why this type of electrode for EEG and Evoked Potential recording is seldom used is that these electrodes have to be autoclaved in order to avoid any possibility of an infection. Additionally, normal plastic insulation does not withstand repetitive autoclaving at 260–270 °F so that the needle electrodes are considered the most unreliable and expensive. For short-term recording, however, when the patient is not moving, one set of needle electrodes made of special platinum alloy could be used.



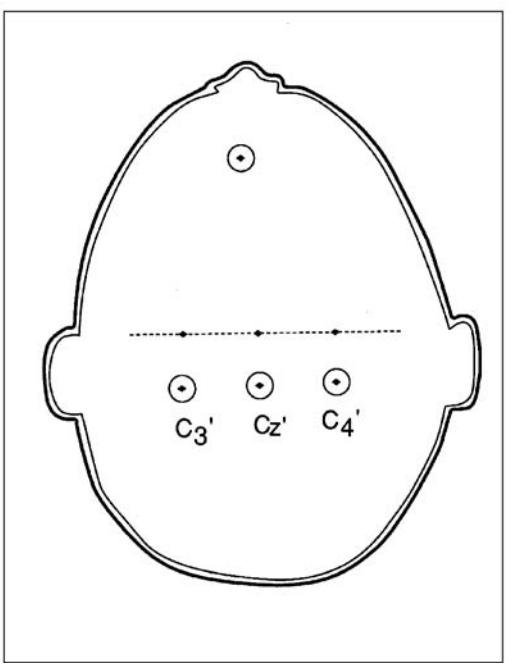


Fig. 27. Electrode locations on the scalp using the 10/20 system where C_3' and C_4' overly the sensory cortex during median nerve evoked stimulation.

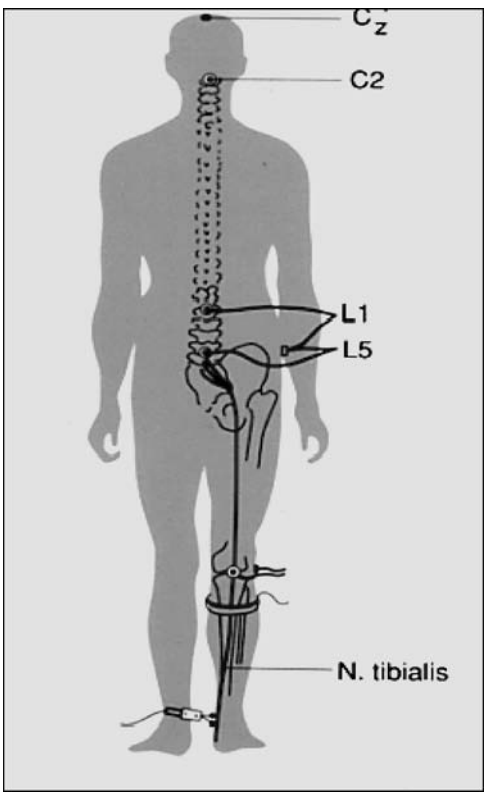


Fig. 28. Position of the Velcro ground strap ground electrode on the leg, and the location of recording sites in posterior tibial nerve stimulation.

INTERPRETATION OF EVOKED POTENTIALS

For practical reasons, an evoked response (waveform) indicates the following:

(a) The sensory stimulus was transduced and conveyed to the brain.
(b) The nerve activity arising from the stimulus reached certain landmarks at certain times.
(c) The time of arrival signifies conduction speed.
(d) The duration of evoked potential can be related to synchronicity of nerve firings.
(e) The number of fibers firing at a given point in time influences the amplitude of the evoked potential.

What however, does an abnormal response mean? An abnormal response indicates:

(a) That the stimulus was either not transduced due to technical problem or a receptor problem,
(b) That the stimulus was not transmitted due to a pathology or interruption in the pathway, or
(c) That the response could not be recorded because of poor electrode contact, too much noise, or a technical problem.

The goal in sensory evoked potential monitoring:
a. Always strive to optimize results,
b. Make the signal as large as possible and
c. Make noise as small as possible.

Considerations in electrode montage and the preamplifier

At least two channels of input should be monitored with every instrument. Thus, the following scheme (Table 4) will outline in which manner the electrodes are connected to the preamplifier input in order to get an appropriate signal.

Before one gets into the operating mode, it is important to undertake an impedance check in order to avoid

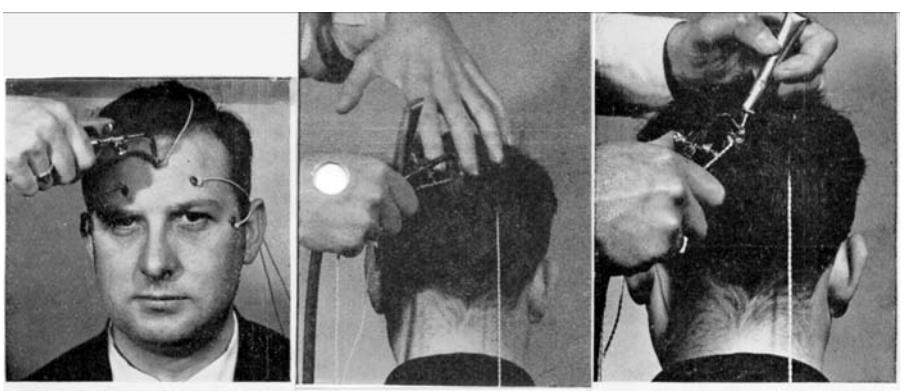


Fig. 29. Fixation of cup electrodes for evoked potential monitoring using collodion and a reciprotor pump which blows air for rapid drying.

Table 4. Summary of electrode locations in SSEP recording of the median and the posterior tibial nerve

	Channel 1		Ground	Channel 2	
Median nerve stimulation					
Left arm	FpZ	C4′	Left arm strap	Left Erb	FpZ
Right arm	FpZ	C3′	Right arm strap	Right Erb	FpZ
Posterior tibial nerve stimulation					
Left leg	FpZ	Cz′	Left leg strap	Left popliteal fossa	2 cm below
Right leg	FpZ	Cz′	Right leg strap	Right popliteal fossa	2 cm below

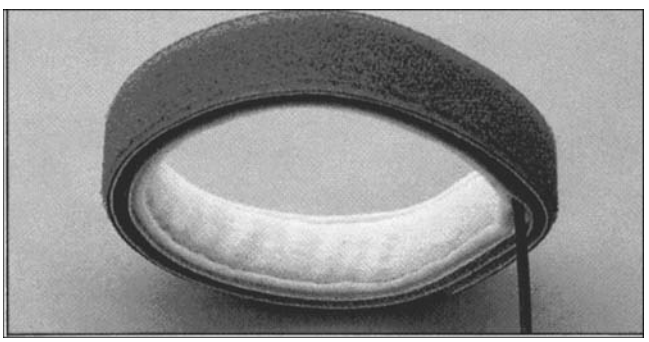


Fig. 30. The Velcro ground strap electrode used for grounding used in evoked potential monitoring.

any lead problems and correct the electrode site if necessary if impedance is 5 kΩ or above. For proper recording, impedance should be around 2 kΩ, an attempt that is equal for all electrodes.

TROUBLE SHOOTING ELIMINATING HIGH IMPEDANCE AND AVOIDING ELECTRICAL NOISE

The following step-by-step procedure is advocated when a recording signal is distorted or high electrical interference is seen on the display:

1. If the impedance is too high in all electrodes, check the ground as it affects all other electrodes.
2. If the impedance is greater than 5 kΩ in any of the electrodes, reinsert the stub adaptor into the hole of the electrode dome, abrade the skin by turning motions and insert some more conductive gel or paste, so as to completely filling out the space between electrode dome and skin.
3. Replace the electrode if the impedance still stays high after attempting to abrade the skin for at least twice. It is necessary to reduce the impedance as much as possible for the following reasons:

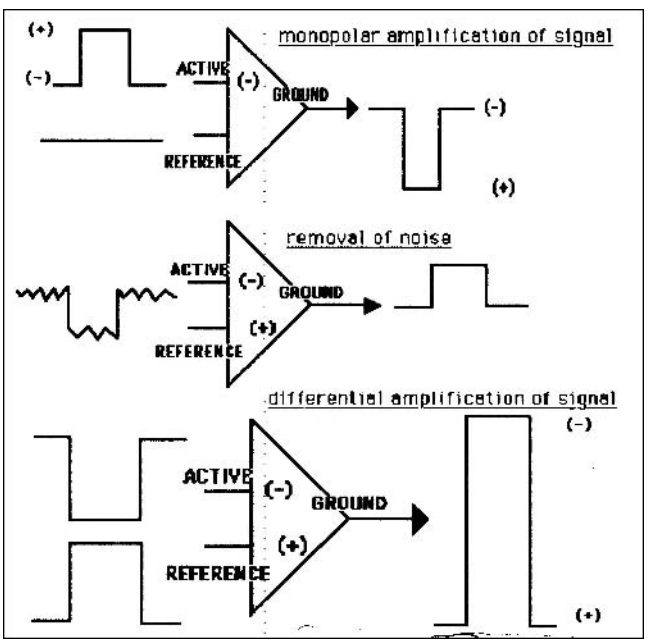


Fig. 31. The basic principles of the amplifier in evoked potential recording.

(a) A high impedance increases noise pickup, since this electrode with its cable will act as an antenna for all sorts of tiny electromagnetic waves in the air.
(b) A high impedance will generate random noise by itself.

Current will flow through the recording electrodes only if this path offers less resistance than the surrounding skin. Therefore, it is mandatory to minimize impedance at the electrode-to-skin connection as much as possible in order to get a signal from the underlying cortex. Transmission of activity through the membranes covering the cortex, the cerebrospinal fluid, the bony scull, and the skin all result in a diffusion of potential changes which ultimately will result in a decrease of amplitude of the evoked potential and a blurred spatial distribution. Thus, in evoked potential

testing, it is always necessary to make the signal as large as possible and to reduce the noise as much as possible. The objective is to minimize noise before it gets into the instrument. Otherwise noise must be reduced within the instrument via filters, signal averaging, etc. The following types of noise should be avoided as they disturb the active signal significantly:

1. Exogenous noise from the environment such as motors (e.g. the respirator), lights in the room, improperly grounded ECG and/or blood pressure monitors, TV screens, 50–60 cycle stimulus artifacts, and sounds from the loudspeaker.
2. Endogenous noise within the patient such as ECG, ERG, EMG, blinks, and muscle twitch.

In order to reach low electrode impedance, the solution is to remove all exogenous source of noise and/or relax the patient. Patient relaxation is important to obtain good evoked potential signals. Sometimes a change in the position of the preamplifier will result in lesser interference with exogenous sources of noise while in another case the machine, which generates the noise, such as the respirator, should be positioned further away from the patient. At times it is also helpful to make sure that the external sources are properly grounded via a third electrode wire. In order to avoid active-to-reference jumper, it is advisable to connect the reference electrode with the ground, as the ground is not a signal path and not an earth ground. Faraday screens are not really a necessity. Another potential source of electrode noise are the wire leads of the active, reference, and ground electrodes. One should keep the following advice in mind:

1. All electrodes are to be made of the same material in order to avoid DC potentials.
2. Leads may act as conductors, working like antennas which pick up electrical noise from the environment. Thus, they have to be kept away from sources of noise and should not be crossed by other leads (e.g. ECG).
3. All leads should follow the same path to the preamplifier.
4. All leads should be of the same length, and should be kept as short as possible.
5. A broken protection insulation in any part of the cable will result in artifacts.

Once the signal is picked up from the electrode and transmitted to the preamplifier via cables, there are a number of options to deal with the incoming electrically distorted signal.

The differential amplifier, an integrated part in evoked potential measurements

The differential amplifier in evoked potential recording is an integrated and important part in reducing noise as it posesses the following capabilities (Figure 31):

1. It amplifies the voltage difference between active and reference lead.
2. It rejects similarities between active and reference input (=common mode rejection).
3. A positive signal at the active input will be displayed downwards.
4. A positive signal at the reference input will be displayed upwards.
5. The differential amplifier is important for noise rejection insofar as

   (a) The impedance of electrodes is lowered,
   (b) The impedance levels between the electrodes is balanced,
   (c) It aids in evaluating the choice of montage, and
   (d) It automatically selects the appropriate amplifier gain for the incoming signal.

Optimizing signal-to-noise ratio in evoked potential monitoring

Avoiding noise in recording evoked potentials

Because noise in evoked potential recording results in poor recording of the event-related potential every necessary precautions should be undertaken in order to minimize noise which is a major cause of bad recoding in the operation room or the intensive care unit.

By definition, noise is comprised of all electrical activity other than the desired signal, which is picked up by the instrument. The objective therefore is to minimize noise before it gets into the instrument; otherwise (and this is less desirable) noise must be reduced after it gets into the instrument using different filter settings, signal averaging, etc. There are different types of noise.

Asynchronous noise, which is not locked to stimulus, may be due to:

(1) Exogenous from the environment of the patient such as motors, lights, TV fields, sounds (talking). The solution is to remove exogenous sources from the recording area and keep the electrode impedances low.
(2) Endogenous, which originates in the patient and is due to the EEG, the EKG, and the EMG. The solution is to keep electrodes away these sources of noise in the

patient by relaxing the patient and keeping impedances low.

Another type of noise is synchronous noise, which is locked to a given stimulus and can be differentiated into:

(1) Exogenous noise of 60-cycle, or a stimulus artifact. The solution is removing the sources of this noise, change the repetition rate of stimulator so it is not a multiple of 60. Ideally, a random stimulation rate should be chosen if it is available. In addition, lower stimulus intensity.
(2) Endogenous, synchronous noise such as links or muscle twitch from the patient. The solution is to relax the patient, lower the stimulus intensity and strive for lower impedance.

The following steps should be undertaken in order to remove ambient electrical noise.

(a) Use a 1 kΩ resistor – active-to-reference jumper connection with reference to ground.
(b) Move the preamplifier around to various positions. Observe noise on EMG mode; widen the filter settings
(c) Position the recording machine (and the patient) away from noise.
(d) Check to be sure that the third wire electrical ground is really ground and neutral.

Filter setting in eliminating noise

Electrical noise and interfering signals contain a random mixture of all frequencies, whereas the evoked potential only contains selected frequencies. The objective in filtering is to remove noise, which does not overlap the signal by blocking it from entering the computer system (Figure 32). The sharp edges as shown in the following schematic diagram (f and f_1) represent the points where noise frequencies

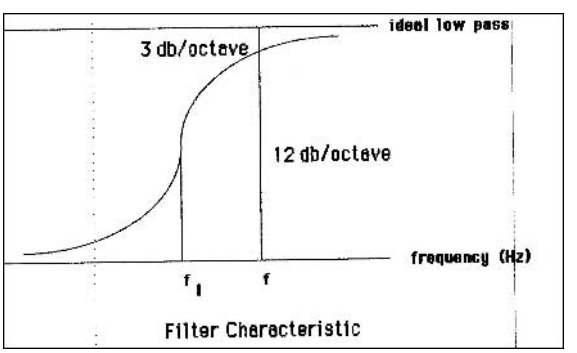


Fig. 32. Basic functioning of a filter to reduce electrical noise in an incoming evoked potential signal.

are attenuated. However, in reality the filter has a gradual slope. For instance at point 'f_1' = 100 Hz cut-off, noise will be 1/4 times as large as at 50 Hz.

Noise is not totally eliminated by filtering, as an increase in the slope of attenuation otherwise would result in twist of the base line. Thus, a filter setting necessary in the analysis of a raw signal is limited by its high- and low-cut. If, however, the filter setting is too steep, this would result in a partial removal of the active signal, an increase in latency and a change in the morphology of the response in evoked potential monitoring.

Processing the signal in evoked potential recording

In order to take advantage of computer technology, the EEG signal in evoked potential recording undergoes several steps before it is viewed on the screen.

Analog to digital conversion. The process of digitization is best described by the sequence: sample, hold, digitize, and label. In discrete steps of time the sampling is fast enough not to miss any change in the spectral event. Thus the higher the sampling rate, the better the resolution and the smoother the changes of the wave. For instance most units have a sampling rate of 2.56 kHz/channel, while on the other hand other units has a sampling rate of 3.1 kHz/channel, which results in better resolution and smoother wave display.

Averaging technique in evoked potential recording

The evoked potential picked up from the scalp ranges from 1–6 μV compared to EEG potentials in which the amplitude ranges from 10–200 μV. For this reason special techniques need to be employed to extract the evoked potential wave from the ongoing background EEG. This technique is called signal averaging. The EEG is a continuous signal, while the evoked potential is a specific, short duration response to the stimulus. Thus the evoked potential is contained in the raw EEG signal. In averaging, the EEG activity during a specified time period immediately following the delivery of the stimulus is analyzed. For analysis, the continuous EEG signal is converted into a series of discrete numbers, each number being proportional to the amplitude of the EEG at that point. The numbers are then stored in specific memory bins in the computer. This is called analog-to-digital conversion. With the delivery of the next stimulus the EEG signal during the specified time period is again digitized, and each point summed with the value previously stored in the corresponding bin, and then stored back into that bin. The general principle of averaging is that if a sum of values is taken that are essentially

random (in this case the EEG signal is considered to be random) the digitized values will be both positive and negative values, and their sum will approach zero. The nervous system, however, responds to a stimulus essentially in the same manner each time, and the sum (average) of these digitized values in each bin will increase (either positively or negatively) to produce a consistent, recognizable waveform. The more samples are used in obtaining the average, the greater the reduction of the background or random noise compared to the evoked potential. Averaging therefore is a signal enhancement technique in which the amplitude of a time-locked neural activity (the evoked potential) is enhanced relative to random activity of the underlying EEG and EMG. As the number of repetitions increases, the effective EEG amplitude decreases, leaving the 'pure' cortical response to the stimulus (Figure 33).

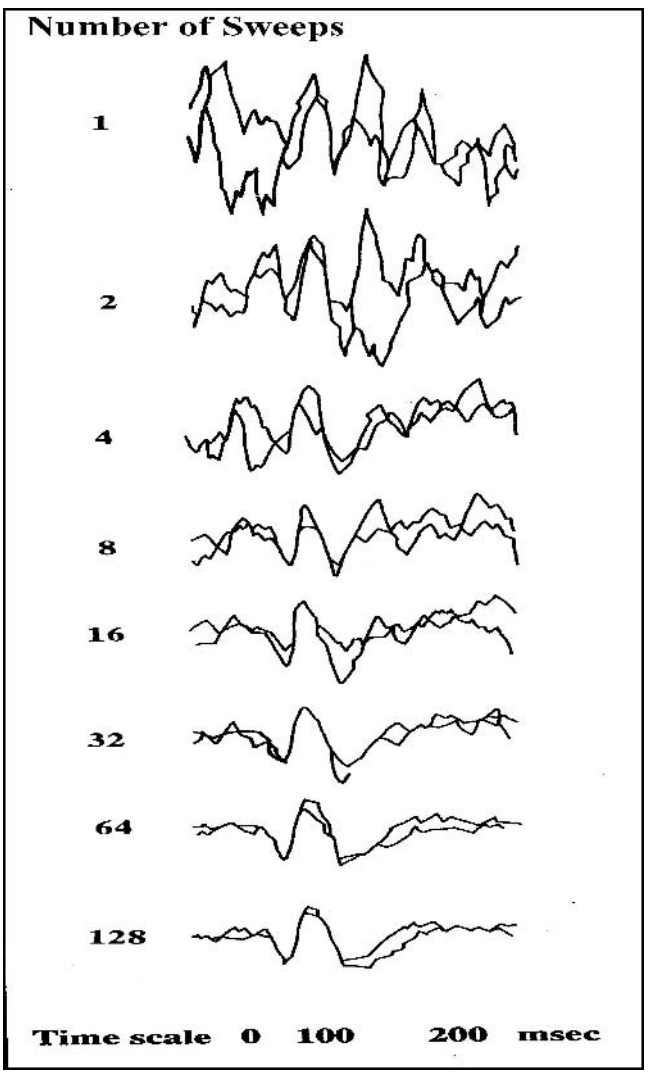


Fig. 33. Principle of averaging in evoked potential monitoring. Note, the higher the number of sweeps being averaged, the better the evoked peak (low signal-to-noise ratio).

Choosing the appropriate stimulus rate

The stimulus rate is the number of times the stimulus is applied to the patient per second. The stimulus may be changed according to the preference of the user. The stimulus rate must not be faster than the analysis time (Figure 34). If the patient is stimulated faster than the sampling time of an EEG epoch, a stimulus artifact will be present in the collected data (backfiring of the stimulus). Most of the units automatically prevent this from happening by limiting the number of stimulus rate options according to the analysis time selected by the user. The longer the analysis time, the slower the rate must be, causing fewer options to appear on the menu. The maximum rate of stimulation may be selected when the analysis time is changed to 50 ms. It is important to note that the stimulation rate as it is selected from the menu is offset by some fraction of rate in order to avoid synchronization with 50 or 60 Hz harmonics respectively (Table 5).

Choosing the correct number of sweeps for averaging

The number of averaging is a parameter, which reflects the total number of stimuli the patient receives to produce an average waveform. This parameter is not dependent on other parameters. Generally, the higher the number of averages (stimulus repetitions), the more noise-free is the resulting averaged waveform. Median nerve and posterior tibial nerve SSEPs can usually be obtained using 256 stimulus repetitions or 512 in a noisy environment. Spinal or cervical responses require considerably more stimuli. The values of stimulus repetitions are set on the keyboard of the evoked potential analyzer and may range from 32 to 64–128–256–512–1024–2048 and 4096 sweeps.

In practice the number of averaging is sufficient:

(a) When the response signal stops changing on the screen and stabilizes, and
(b) The results can be replicated and are consistent.

Choosing the appropriate analysis time

The analysis time is the duration in the EEG (in msec), which follows each stimulation and where the unit collects the data and uses them to calculate the average waveform. The analysis time determines the maximum horizontal time scale able to be analyzed on the display. This time

Table 5. Summary of the selected stimulus rate and the actual slight offset being done automatically by the evoked potential unit

Stimulation rate	Actual rate (60 Hz)	Actual rate rate (50 Hz)	Stimulation rate	Actual rate (60 Hz)	Actual rate (50 Hz)
1	0.992	0.990	6	5.714	5.882
2	1.967	1.961	7	7.059	6.818
3	2.927	3.030	8	8.000	8.000
4	3.871	4.000	9	9.000	9.091
5	4.800	4.762	10	10.345	10.417

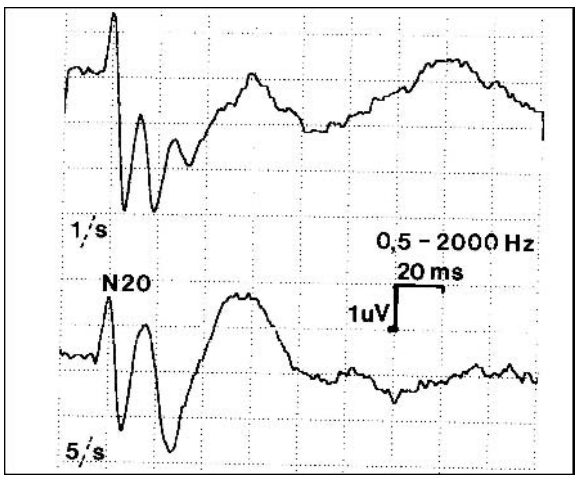


Fig. 34. Difference in stimulation rate (top 1 Hertz, bottom 5 Hertz), which affects the appearance of the late peak in evoked potential recording.

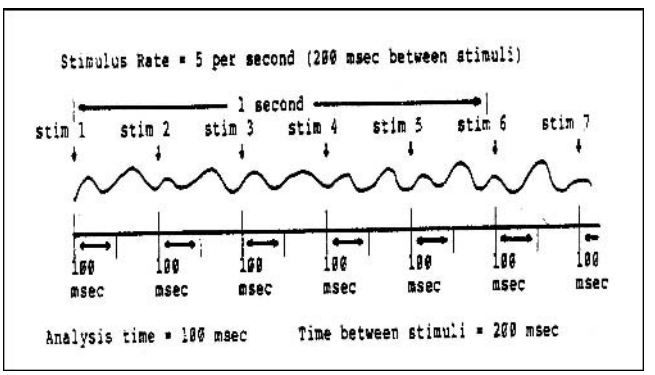


Fig. 35. Stimulus and recording parameters in relation to the raw signal of the EEG. If stimulation is 5/s there is a 200 ms time span necessary between each stimulus (1/5 = 200 ms). The time before another stimulus can be averaged is 200 ms.

must be set so that the peaks of interest of the wave fall within this time. If a time is selected which is incompatible with the chosen stimulus rate, a message will warn the user and the rate is changed to be compatible with the analysis time (Figure 35). The analysis time, which usually can be selected ranges from 80 to 100–150–200–250–300–400 and 500 ms.

Locating the optimal stimulation site

In order to properly locate the optimal stimulus site on the skin overlying the superficial nerve, such as in median nerve recording, the patient's hand should be placed palm-up and in a natural relaxed position. The inner surface of the wrist has to be wiped with alcohol to remove any skin oils. Thereafter, the area has to be dried completely with a clean gauze square. The alcohol has to be wiped away as otherwise it will break down the conductive gel of the stimulating electrodes. The nerve to be stimulated is now located with the additionally supplied bar stimulator. For median nerve location the tendon that runs down the wrist approximately in the middle of the arm is located. The median nerve is usually found at the wrist adjacent to the large tendon, which runs from the middle of the arm from the elbow towards the little finger of the hand (Figure 36).

For posterior tibial nerve location, the inside ankle, between medial malleolus (ankle bone) and Achilles tendon has to be stimulated (Figure 37). The patient should always be informed that a selective site is going to be stimulated and he or she will begin to feel some pulses at the wrist/ankle. Begin at very low level and increase gradually until the thumb/toe twitches. The stimulating bar is now placed over the median/posterior tibial nerve with the cathode (the negative electrode usually colored red) located proximally. Then the bar stimulator cable is plugged into the stimulating device and intensity is slowly turned on. The pulses will be delivered at a rate of 1 per second. Usually a pulse light next to the digital display will flash each

Table 6. The parameters usually chosen for SSEP analysis

Parameter	Median nerve	Posterior tibial nerve
Stimulus rate	5/sec	5/sec
Analysis time	50–150 ms	100–300 ms
Number of sweeps	256 (or 512)	256 (or 512)

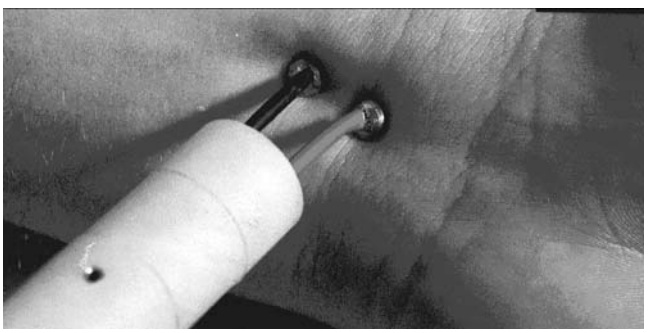


Fig. 36. Location of the median nerve using the bar stimulator placed over the medial part of the wrist.

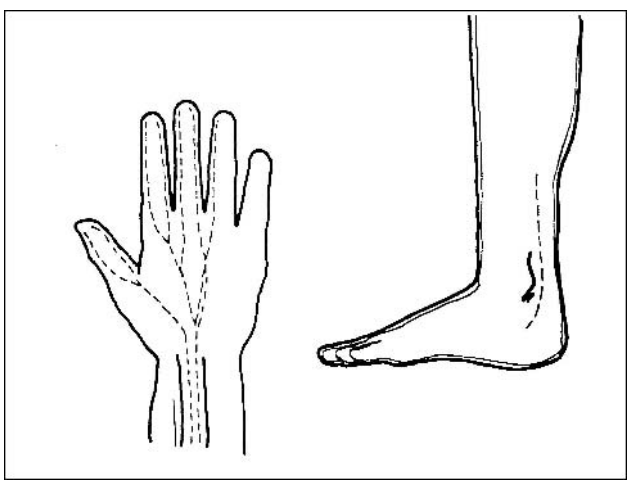


Fig. 37. Location of median (left) and the posterior tibial nerve (right) for the exact application of stimulating electrodes.

time a pulse is delivered. While the current is being increased, the patient is asked where he/she feels the pulse. For the median nerve, the patient should feel the pulse travel down into the hand towards the thumb and the index finger. The pulse should not be felt in the little finger, as this is the ulnar nerve. For posterior tibial nerve the pulse should travel down the sole of the foot to the toes. If the pulses are felt in the heel, the stimulus is over the wrong branch of the nerve. Then the stimulating bar electrode is moved in order to find the optimal stimulus location. One may exert some pressure on the bar, as the nerve sometimes is located

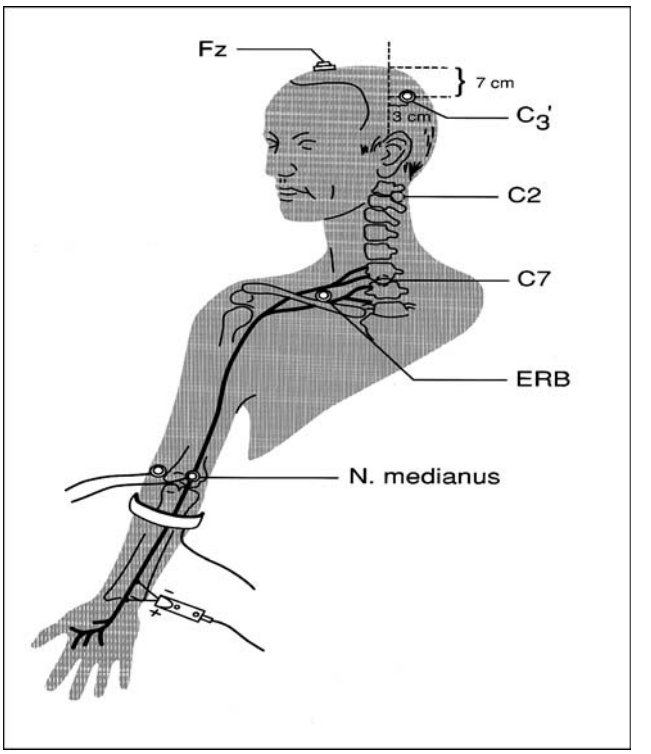


Fig. 38. Alternative sites for recording during SEP monitoring (Erbs point, cervical C VII and C II), during median nerve stimulation, position C VII is useful in recording the entrance of the signal into the spinal cord.

deep below the skin. Conductive gel is applied on the site of the stimulating electrodes to prevent burning of the skin. One electrode should not connect with the other electrode as this causes a 'salt bridge' shorting out the stimulus. Once the pulse is felt in the correct location the stimulus intensity is slowly increased until the thumb/toe twitches.

The stimulus intensity, as flashed on the display at which the thumb/toe twitches, is noted and remembered for later stimulation. Thereafter the stimulator is switched off, the bar removed and the indented circles which are shown on the skin from the pressure of the bar electrodes wiped with alcohol and dried completely. Thereafter pre-gelled pediatric ECG electrodes are applied on the stimulation site, one on each circle left by the bar electrodes and connected with the stimulator cable. One always has to remember that the cathode (usually marked red) is located proximally. When using ECG pad electrodes, a few mA may now increase stimulus intensity since no pressure is being applied (Figure 38).

Alternating recording and stimulus sites

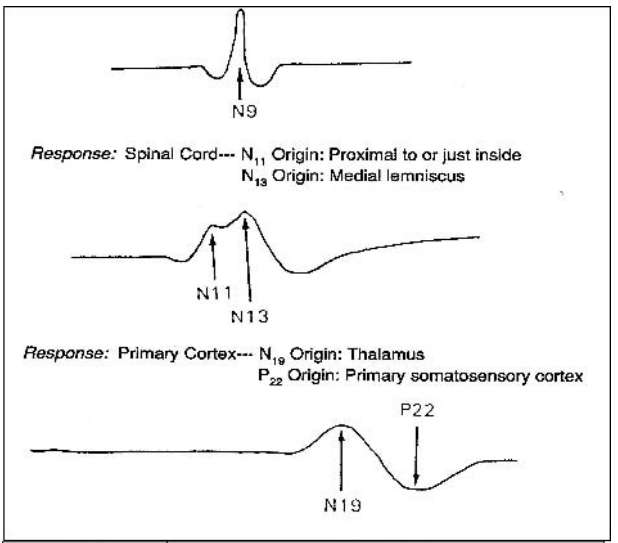
Somatosensory evoked potentials can be recorded with a varying degree of success from just above any site over

the nerve being stimulated. The recording site depends very much on the operation that is being done, and the nerve structure being at risk. Alternate sites of recording include:

(a) The cervical cord, usually the skin overlying the proc. spinosus of C7 and/or C2 (Figure 38), and
(b) Any position along the spinal cord during posterior tibial nerve stimulation. Evoked potentials recorded along the spinal cord are called Spinal Evoked Potentials (for further details see chapter III on Spinal Evoked Potentials).

Another alternating stimulating site is the common peroneal nerve. It crosses the head of the fibula and presents another common site for stimulation. Sometimes it is impossible to stimulate at the location specified above. Alternative sites may be found by moving up the nerve to the next superficial location. For example, if the median nerve is inaccessible, the stimulating electrodes may be placed in the antecubital space or the popliteal fossa in tibialis posterior recording.

Table 7. Summary of the purported generators of short-latency SSEPs. Adapted from [9]



Peak	Generator
N_9	Brachial plexus
N_{11}	Spinal roots of dorsal horn
$N_{13} + N_{14}$	Spinal gray matter of dorsal column
N_{20}	Primary somatosensory cortex

Alternating recording electrodes

Besides silver/silver chloride cup electrodes, platinum or stainless steel needle electrodes can be used successfully for recording in the operating room. The reason for their use is the ease of their application. However, when using needle electrodes, special care has to be taken to secure the electrodes with tape to the skin and avoid any kind of strain so as not to pull the electrodes out. Needle electrodes can also be used for recording from such places as Erbs point which can also be used as stimulating electrode site.

In summary, during median nerve evoked potentials, generally two recording sites are used, one site on the peripheral nerve and the other side over the corresponding hemisphere (Table 7):

1. For the evaluation of functional integrity of the peripheral nerve Erbs point is used.
2. For the evaluation of cortical and subcortical integrity either C3 or C4 respectively.
3. In certain cases with the possibility of cervical trauma central conduction time (CCT) is derived using an additional electrode over the cervical spine at position C7.

In addition for recording, needle electrodes can also be used for stimulation. When needle electrode is used for stimulation, the stimulus current necessary to obtain muscle twitch, is much less than the current usually necessary with pre-gelled pad electrodes. This is because the skin acts as an insulator, which is drastically reduced with needle electrodes as the current is applied close to the sensory nerve.

After recording stimulation and recording electrodes have to be removed. The following procedure is recommended for removing electrodes (stimulating or recording) from the patient:

1. Soak a cotton ball with acetone.
2. Hold the cotton ball into a gauze square and wait about 15 seconds for the acetone to absorb into the gauze.
3. Wipe the gauze across the electrode, allowing removal of the electrode and the gauze from the scalp.
4. Wipe the remaining collodion, electroconductive gel, and acetone with a clean, dry gauze pad until the site is reasonably clean and dry.
5. Repeat the above steps for each electrode attached with collodion.
6. Remove the stimulating disk electrodes.
7. Remove the ground strap(s).
8. Wipe off remaining electro-conductive gel at electrode sites with alcohol.
9. Recheck the scalp for remaining collodion, remove it by using gauze with acetone.

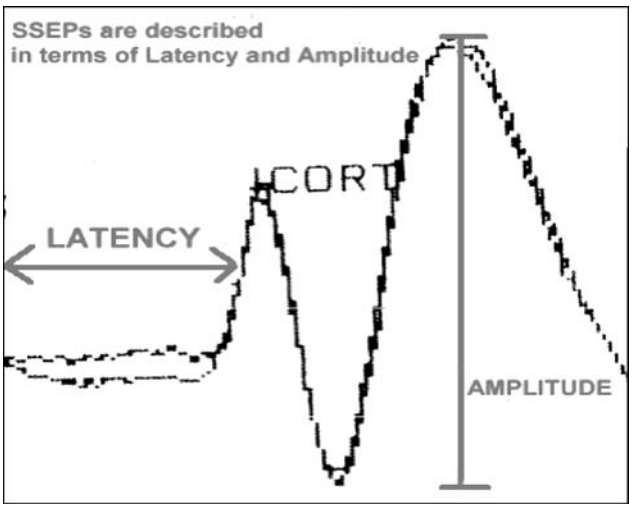


Fig. 39. The relevant information contained in an evoked potential, i.e. latency and amplitude height and how they are measured.

EVALUATING THE RESPONSE OF THE EVOKED POTENTIAL

As peripheral nerves, nerve plexus, nerve roots, and dorsal columns of the spinal cord transmit somatosensory evoked potentials, they follow the lemniscal pathway to the thalamus and the primary sensory cortex. The ascending volley of electrical activity can be picked up from any of the several sites along this pathway. A characteristic waveform is generated as the impulse passes under each of the active electrodes placed along the nerve pathway. The resulting waveforms are named according to the polarity of the signal as the body generates them. N for negative, and P for positive resulting in amplitude (measured in μV), and the approximate time (latency in milliseconds; ms) it takes for that response to occur after the stimulus (Figure 39).

Evaluation of median nerve evoked potential recordings

Conduction velocities in peripheral nerves can be recorded by measuring the nerve action potentials that arise in nerve trunks and in the brachial and lumbar plexus. These early EPs are important as they conform an adequate sensory input when the function of higher CNS centers has to be evaluated. A negative potential recorded from the skin overlying the second cervical spine will appear about 14 ms post median nerve stimulation and is thought to arise in the dorsal column nuclei. A typical evoked potential as recorded over the specific sensory cortex, contralateral to the site of stimulation, as seen in the following figure shows traces obtained from stimulation of the median nerve at the wrist. The first electrode detecting the impulse is

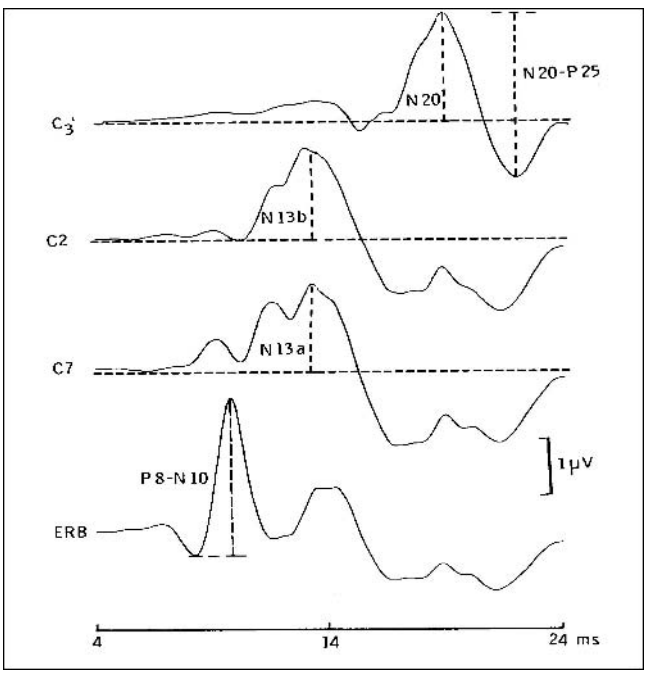


Fig. 40. Median nerve evoked potentials with recording at Erbs point (EP), the cervical spine at C7, C2 and at the scalp at position C_3'.

over the brachial plexus at Erbs Point (Figure 40), generating a nerve action potential, generally called N_9. The impulse continues, entering the spinal cord and ascends in the dorsal columns to synapse in the brainstem nuclei. A second neuron originates in the brain stem and travels to the thalamus, where it synapses. A third neuron originating in the thalamus projects to the sensory cortex resulting in the waveform detected by the electrode placed over the sensory cortex. The thalamus/thalamocortical radiation response is initially negative, called N_{20} and is followed by a large physiologically positive potential, called P_{25}.

Some observers postulate the N_{20} wave to originate in either the thalamus or the thalamocortical radiation [7]. By convention this wave is labeled N_{20} where the letter designates the polarity and the number indicates the minimum poststimulus latency of 20 ms. All observers, however, agree that the preceding waves seen after stimulation and which are distributed widely over the scalp are of subcortical in origin [6, 8] (Figures 40 and 41).

The following Table 7 summarizes the purported generators of short-latency somatosensory evoked potentials, which play an important part in evaluating the function of deeper brain structures.

The non-specific response of the later evoked potentials (over 50 ms) is generated in the primary sensory cortical area and' their associative centers. Pathological changes at any point along the conducting pathway from the site of

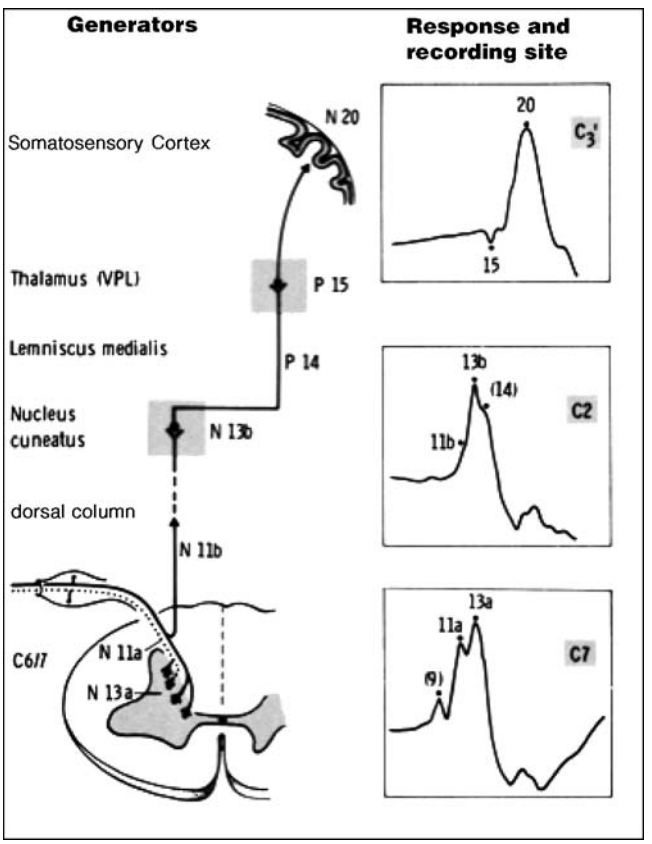


Fig. 41. The various peaks as they are generated during median nerve evoked potential stimulation at the spine and the cortex.

stimulation to the specific somatosensory cortex can affect the SSEP [10]. A localization of lesion is often possible if early peaks are present and stable, but later peaks are absent or abnormal. Thus, SSEPs serve to detect pathology, localize the deficit, and in a limited way, gauge severity and character of the disorder (Table 8).

With median evoked potentials it is possible to localize the site of a possible functional disorder in the somatosensory pathway by the absence or delay (Abs) of the peak at the corresponding recording site.

Evaluating the potential in posterior tibial nerve stimulation

Because of the greater distances, SSEPs elicited by stimulation of the posterior tibial nerve at the ankle, have greater post stimulus latencies than the SSEPs generated by stimulation of the median nerve at the wrist. While the initial negativity at the cortex appears approximately 20 ms after median nerve stimulation, latency of the initial negative peak after posterior tibial nerve stimulation will appear at about 30–40 ms post stimulus.

In recording the posterior tibial nerve evoked potential some technical problems arise if the forehead reference is used. The length of the sensory nerve pathway from the ankle to the brain introduces a lot of 'artifacts' from the electrical fields generated by other parts of the body. This makes it more difficult for the small potentials to be recorded as they are generated in the sensory nerve pathway. In order to record the peripheral nerve action potentials, the 'active' electrode is placed over the popliteal fossa (PF) at the knee ipsilateral to stimulation and the 'inactive' electrode is placed below and slightly to one side of the PF about 3 cm away.

The SSEPs during posterior tibial nerve stimulation reflect the arrival of nerve volleys at specific landmarks along the sensory pathway resulting in interruptions and delays which can be detected and localized. When measuring stimulation response over the lumbar spine, N_{20} originates in cauda equina and dorsal root entry. It is used as reference point for measurement of central conduction velocity. Thus, not only the pathology and the localization of a deficit may be identified, but in a limited way, these SSEPs also gauge the severity and the character of the disorder (Figure 42; Table 9). The figure below shows the traces from stimulation of the posterior tibial nerve at the ankle. As the impulse travels up the leg, a characteristic nerve

Table 8. Summary of the different location in sensory disorder and results as they are visualized in the SSEP during median nerve stimulation. Abbreviations: Abs = absent or delayed; N = normal; Stim = stimulus

Location of potential disorder	Peripheral nerve	Erbs point	N_{11}	N_{13}	N_{20}	P_{25}	Interpeak latency increase
Peripheral nerve	Abs	Abs	Abs	Abs	Abs	Abs	Stim-Erbs point
Brachial plexus	N	Abs	Abs	Abs	Abs	Abs	Stim-Erbs point
Spinal root	N	N	Abs	Abs	Abs	Abs	Erbs-N_{11}
Brainstem	N	N	N	Abs	Abs	Abs	N_{11}-N_{13}
Thalamus	N	N	N	N	Abs	Abs	N_{13}-N_{20}
Cortex	N	N	N	N	N	Abs	N_{20}-P_{22}

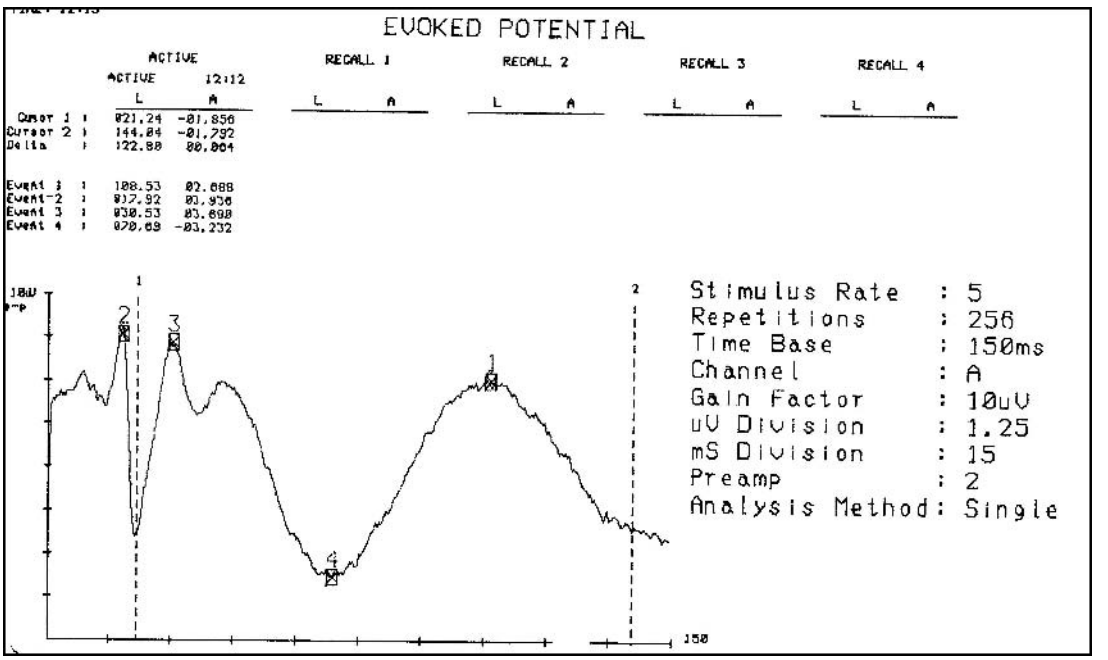
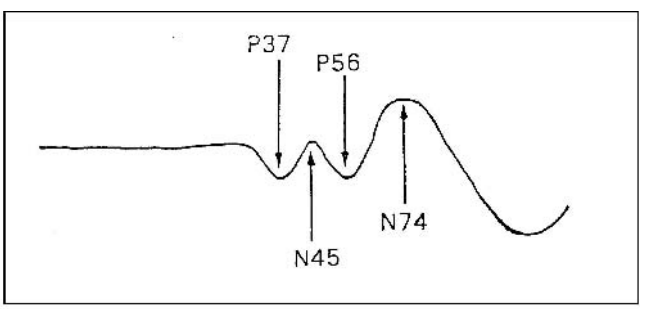


Fig. 42. Typical recording of median nerve SSEPs at the scalp with normal configuration. Note the specifications of stimulation on the right. By cursor positioning the peaks can be identified, computing automatically amplitude height (μV) and latency (ms).

action potential is generated as the impulse passes under the electrode at the popliteal fossa, usually designated Ns. The impulse continues, entering the spinal cord, ascending towards the brain in the dorsal columns to the sensory neuron synapses in the brainstem. A second order neuron originates in the brainstem and ascends to the thalamus. From the thalamus a third order neuron originates and is projected to the sensory cortex. The thalamo- to thalamocortical radiation potential (Figure 43) is initially negative and called N_{33}. This is followed by a large positive potential, called P_{37}, with another large negative potential following, called N_{45}.

Table 9. Summary of the various peaks as they are generated during posterior tibial nerve stimulation and the different location in sensory disorder as they are visualized in the SSEP during posterior tibial nerve stimulation. Abbreviations: Abs = absent or delayed; N = normal; P_{37} = Peak recorded at Cz′ with a latency of 37 msec



Location of potential lesion	Peripheral nerve	Lumbar spine	P_{37}
Peripheral nerve	Abs	Abs	Abs
Spinal root	N	Abs	Abs
Spinal cord and brainstem	N	N	Abs
	N	N	Abs

CRITERIA FOR ABNORMALITIES IN BOTH MEDIAN AND POSTERIOR TIBIAL NERVE EVOKED POTENTIAL

There are typical criteria in sensory evoked potential monitoring, which point to a lesion within the sensory pathway:

1. A shift to the right (increase) in latency of the cortical potential, related to the surgical procedure, which does not return to the pre-surgical baseline when conditions are returned to a pre-shift situation.
2. A total loss of the cortical potential when related to the surgical condition.

Once a difference between subject parameter and normal parameter is evident, a functional deficit has to be suspected. The difference may be in regard to an increase in latency or a depression in amplitude of the specific peak

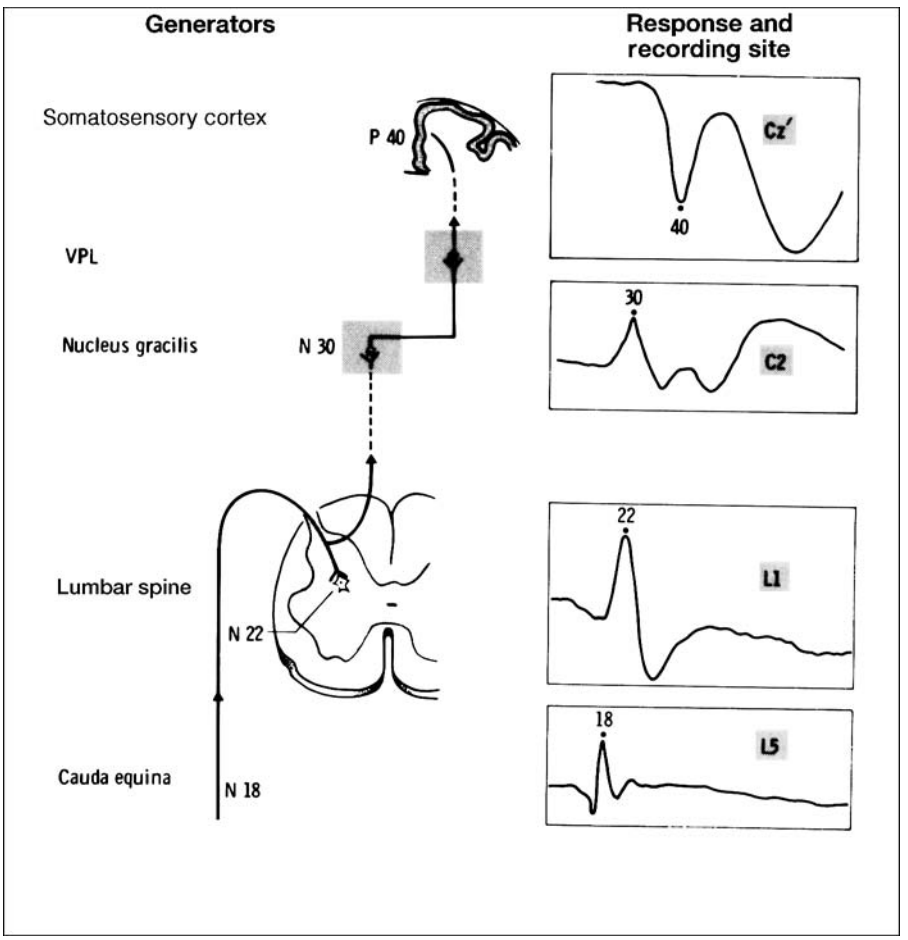


Fig. 43. Location of generators in posterior tibial evoked potential recording. Response of late P_{37}, N_{46}, P_{66} and N_{74} during posterior tibial nerve stimulation. Over the cortex P_{37}/P_{40} is generated in the primary somatosensory cortex, while the other peaks originate in higher cortical areas.

reflecting a slowing in transmission speed or a functional deficit in the specific somatosensory pathway. As evoked potentials are a statistical measured differences, which fall within the range of ± 3 standard deviation (SD = 99%) they present no pathology. Thus, a 50% change in any of the parameters (latency, amplitude height) would indicate a pathologic state. Before interpreting abnormal results, one should reconsider and check the following:

1. Is the evoked potential test pathologic in relation to the other diagnostic measures (blood pressure, anesthetic depth etc.)?
2. Reconsider the limits of the method; it is only a measure of the functional deficit in the nervous pathway. By no means is it a method intended to give a final diagnosis in regard to the underlying pathology (e.g. tumor, intracerebral bleeding, hypoxemia etc.).
3. The quality of the answer depends very much on the specificity of the question. As non-specific response peaks generally are suppressed first with anesthetic agents, particularly the late negative potential may completely disappear, it is not useful to judge hypoxemia during a change in anesthesia using the late evoked potential. In this case, the early-evoked response remains unchanged even at deeper planes of anesthesia and may even be present in case of barbiturate anesthesia when the EEG has completely disappeared.

The following considerations during evoked potential judgment have to be undertaken:

1. If the waveform is indistinguishable:
   (a) Increase stimulus intensity slightly,
   (b) Decrease repetition rate, and
   (c) Check electrodes and instrument settings.

2. Once there is too much random noise to get a good signal:

   (a) Increase the number of averages (sweeps),
   (b) Relax the patient (if awake),
   (c) Check if all other electrical instruments are properly grounded, and
   (d) Check if electrical cables do not run over or under the evoked potential electrodes.

3. Check for stimulus factors that might alter the response:

   (a) Usually there is a better response on electrical than on tactile stimulation.
   (b) Any increase in stimulus intensity will result in no change of latency. However, the amplitude increases as intensity increases during thumb twitch.
   (c) Filter setting will affect the signal. Thus, the use of a low-cut filter not higher than 10 Hz is recommended (Figure 44). A high-cut filter, however, can go as low as 500 Hz if necessary. In some devices filter setting is done automatically.

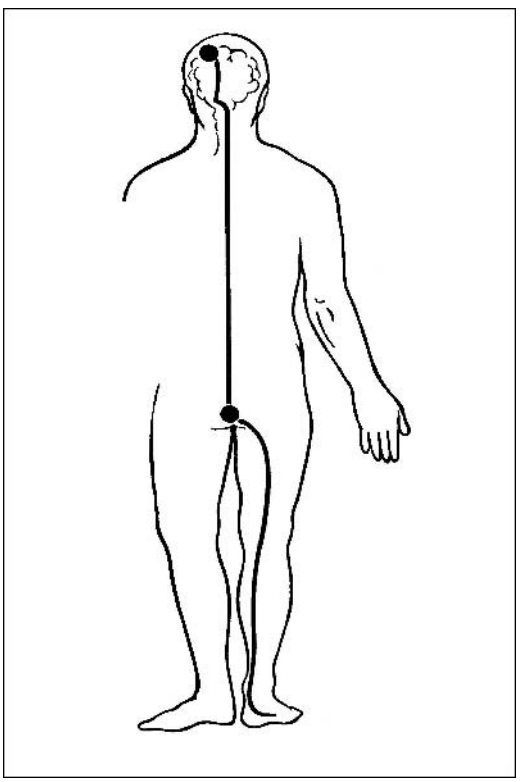


Fig. 44. Generator and localization of the site of functional impairment by recording the peaks at corresponding anatomical sites of the sensory pathway during posterior tibial nerve stimulation.

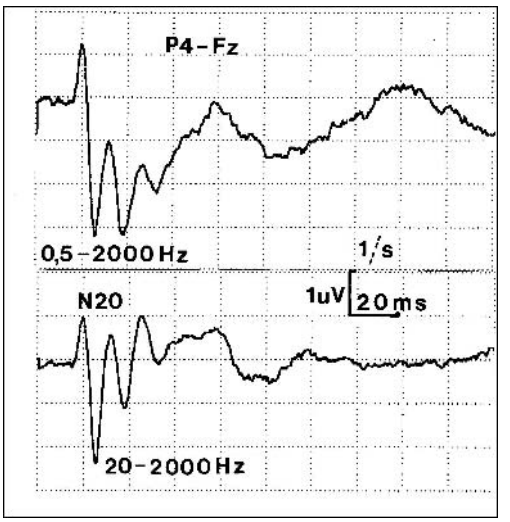


Fig. 45. Different filter setting affecting the late peak of the median evoked potential.

4. Non-pathological factors can alter the response:

   (a) Age: Peripheral nerves age earlier than central nerves; in median nerve conduction slows by approximately 0.16 m/sec/year, whereas central conduction velocity remains stable up to the age of 60 and then slows by 0.78 m/sec/year. Age normally also is correlated with a reduction in amplitude height (Figure 46).
   (b) *Infants*: The interpeak latency shortens rapidly from age 0–2. Later peak latency shortens slowly over the age 2–6 establish themselves around the age of eight (for adult values see Table 2).
   (c) *Gender*: The latency change for females is shorter by 1 ms than that for males.
   (d) *Body temperature*: In the limbs, higher temperature will result in a faster conduction. This increase has a rate of 5% per 1 °C. Cooling of the entire body as in cardiovascular surgery, will affect both the peripheral and cortical potentials, with a progressive increase in latency and a decrease in amplitude of all components. In severe hypothermia a total loss of all peripheral and cortical potentials can be expected. With rewarming, a progressive increase in amplitude and a decrease in latency will occur. Cooling of just the spinal cord at the surgical site will not affect the peripheral potentials, but the cortical potential will show a progressive increase in latency and a decrease in amplitude, which reverses with rewarming.
   (e) *Sleep*, level of *consciousness*: Some effect on the late SEP may be noted.

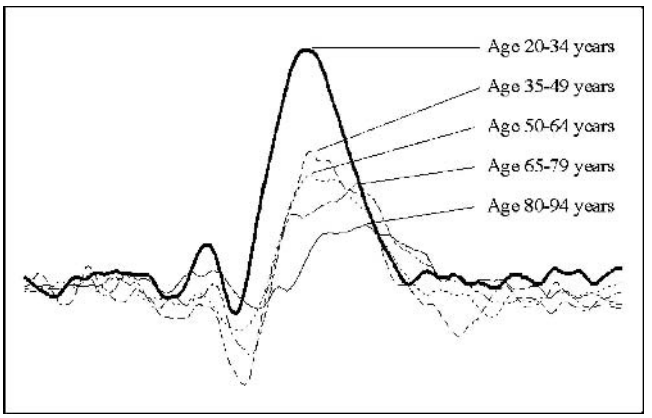


Fig. 46. Amplitude height of the evoked potential, which is reduced with increasing age.

THE EFFECT OF ANESTHETICS ON THE EVOKED POTENTIAL

Among the several factors unrelated to surgical manipulation that will cause changes in the evoked response, besides cooling of the entire body, anesthetics have the most depressant effect. With the induction of anesthesia, an increase in latency of a few milliseconds is expected in the cortical response. But the peripheral response (i.e. Erbs point, popliteal fossa) should not change. The cortical evoked response stabilizes once anesthesia is maintained. Some of the anesthetic agents will have a marked depressant effect on the cortex with increasing dosages. Most notable in their effects with increasing concentrations are the inhaled halogen agents (enflurane, isoflurane, halothane, etc. Figure 47), high doses of barbiturates, benzodiazepines (diazepam), and narcotic analgesic agents (fentanyl, sufentanil, alfentanil etc.). The peripheral evoked potential will show no change, but the cortical evoked potential will show a progressive increase in latency, broadening of the complex, and a decrease in amplitude related to the dose of the agent. These effects reverse with a decrease in anesthetic plasma concentration, especially when there is a decline in the biophase, i.e. the concentration at the receptor site. Peripherally acting neuromuscular blocking agents (NMBAs) such as curare, pancuronium, atracurium, vecuronium, etc. will not affect the SEP responses when used in clinical dosages. However, local anesthetics, when used for plexus blockade, will prevent the impulse from traveling up the spinal cord. Such an effect can be observed in posterior tibial nerve stimulation with spinal or epidural local anesthetics, or blockade of afferent volleys during median nerve stimulation when axillary block is initiated.

When using evoked potentials in the OR and in the ICU, one should observe the following considerations:

1. Replicate the response in order to look for consistency and verify the finding. If in doubt, only the replicated response may be used for the evaluation of peak latency and amplitude measurements.
2. When measurement of conduction velocity is desired:
   (a) Measure the arm length with the arm extended to 90° at the shoulder,
   (b) Measure from the negative stimulus electrode to the C2 vertebra in cm, and
   (c) Calculate nerve conduction velocity in the extremity using the following formulation:

$$\text{Conduction velocity (cm/s)} = \frac{\text{arm length (cm)} \times 10^6}{\text{Latency of potential at Erbs point (ms)}}$$

Summary of SSEP monitoring in the clinical setting

During surgery, SSEPs are useful in many situations such as:

1. In neurosurgery with operative retraction and manipulation around the spinal cord such as tumor or nucleus pulposus prolapse (NPP) resection.
2. In vascular surgery during cross clamping of the abdominal aorta during operative correction of a thoracoabdominal aortic aneurysm (TAA) repair, where perfusion of the spinal cord via the Adamkiewicz artery is endangered.
3. In orthopedic surgery where the spinal cord may be at risk such as Harrington rod insertion and removal.
4. In vascular surgery, for instance during carotid endarterectomy (CEA), where clamping of the artery may result in cerebral hypoxia.
5. In neurosurgery during cerebral aneurysm clipping, where the clip may endanger sufficient blood flow to other parts of the artery.
6. In cardiac surgery, with deliberate hypotension during cardiopulmonary bypass, in order to avoid episodes of malperfusion of the brain.
7. For the evaluation of peripheral nerve lesions.
8. For determination of sufficient intraoperative analgesia.
9. Central sulcus identification during neurosurgery.

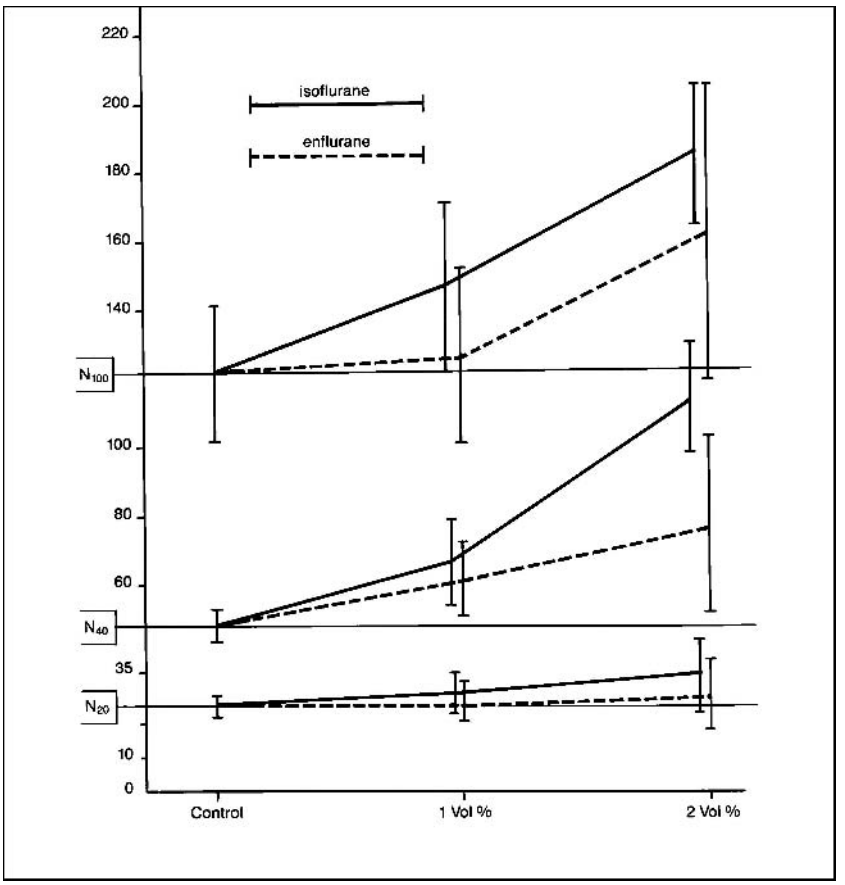


Fig. 47. Summary of patterns of different peaks within the SSEP following increasing concentrations of either isoflurane (n = 10) or enflurane (n = 10) in patients undergoing CABG. Note the significant increase of latency of the late component.

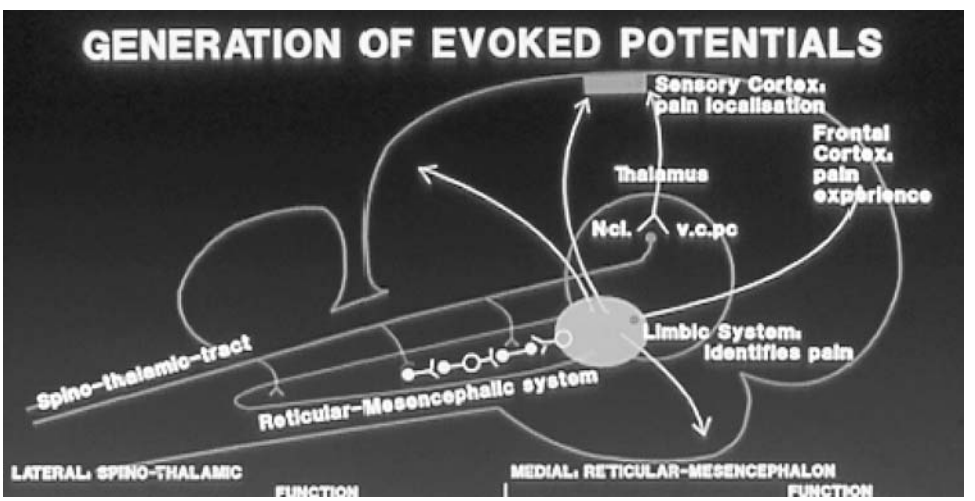


Fig. 48. Determining the antinociceptive level in patients during anesthesia and the specific afferents conveying a nociceptive input to the brain (Nucl.v.c.p.c = nucleus ventrocaudalis parvo-cellularis).

MONITORING ANTINOCICEPTIVE EFFECTS IN GENERAL ANESTHESIA

While the goal of general anesthesia is loss of consciousness, this in general does not comprise a sufficient level of analgesia This question is of special interest because it is known that most anesthetics do not inhibit nociceptive activity, i.e., they do not have any antinociceptive properties.

With most anesthetics, the nociceptive input elicited by surgery is continuous and reaches central structures in the midbrain, thalamus, and the cortex, as demonstrated in numerous experiments [20, 21]. Experiments done in laboratory animals, have demonstrated that the ascending reticular afferent system is partially modulated by anesthetics, causing a decrease in alertness and inducing unconsciousness. The action of volatile anesthetics therefore is of nonspecific nature. Anesthesia causes a loss of experience, particularly the experience of pain, as well as loss of memory and consciousness. In addition, anesthetic agents influence motor control and autonomic nervous mechanisms, modulating cardiac and respiratory functions, blood pressure and blood circu1ation to the brain and body. Although these effects on vegetative parameters are "side effects" which accompany the main effect of an anesthetic, clinically they are used to monitor the depth of anesthesia. Yet the question which of these parameters reflects the degree of pain relief remains unanswered. Since the past decade, spectral analysis of the spontaneous EEG has been used for monitoring the depth of anesthesia. Also, it is well known that the EEG is characteristically modified in deep sleep and gives some evidence on the state of arousal or alertness, reflecting the level of vigilance of the patient receiving an anesthetic. In fact, EEG changes are directly related to changes in electrical activity of the cortex. However, rhythmic potential fluctuations in cortical centers driven by excitatory input from specific thalamic nuclei. Such actions, in turn are influenced by the midbrain and the brain-stem reticular formation, which are the main sites of action of volatile anesthetics. Contrary, opioids directly affect the pain modulating and pain discriminating centers within the CNS, especially via the nucleus limitans, an accumulation of neurons, which lie close to the nucleus ventrocaudalis-parvocellularis (Nucl. v-c. p-c; Figure 47) an area, which is responsible for the recognition of pain.

Many anesthetics presumably act by regulating the serotonin and noradrenalin release control mechanism in the Raphe and the locus coeruleus. Such nonspecific effect is not seen with opioids. For these reasons, it is likely that the spectral density of the continuously recorded EEG gives information about the functional state of the brain under general anesthesia [12]. While different anesthetic agents produce different EEG patterns, with increasing concentrations the power in the spontaneous EEG is usually shifted toward lower frequencies. On-line EEG analysis in the operating room therefore facilitates the individual tailoring of anesthetic doses to patient needs [13]. On the basis of the observation that factors in the spontaneous and evoked EEG differentiate between specific pain-reducing and nonspecific sedative analgesic action, the peristimulus EEG segments was linked to intracutaneous stimuli in healthy volunteers using low-dose ketamine (0.25–0.5 mg/kg). Clinically thus often is sufficient to provide adequate analgesia with inducing a major anesthetic effect. The evoked potential demonstrated a close correlation with individual pain ratings not only with ketamine, but also using opioids like tramadol or the potent analgesic agent fentanyl and a heat stimulus (Figure 50) for evaluation analgesic efficacy [14, 15].

The analgesic component of 36 mg of ketamine, as derived in both variables, corresponded to that of 100 mg of tramadol, a weak opioid. Interestingly, pain-relevant brain potentials did not completely disappear during a ketamine-induced state of unconsciousness. When low-dose ketamine was given without verbal reports of pain, the brain potentials indicated an incomplete analgesic. This effect was comparable with sole use of 1% halothane if the usual N_2O admixture was omitted [16]. Such data suggest that the subjects might have perceived nociceptive activity but could not report it, and in all cases could not remember it. This is an example of the use of evoked brain potentials to assess pain in patients, where verbal reports of pain are not available, such as during regular volatile anesthesia where due to the actions of the surgeons, there is a constant change in nociceptive input. Whether these methods also can be used to explore pain experience in the neonate needs further exploration, since cerebral pain-processing mechanisms in the newborn is expected to be different from those of adults. This is because of the incomplete myelinization of nociceptive afferents and projection tracts.

Aside from intracutaneous stimuli, SSEPs also can be used during routine intraoperative monitoring where electrical stimuli result in an activation of Aδ- and C-fibers. This demonstrats the sufficient blockade of sensory efferent stimuli, which are cued by nociceptive stimuli evoked by the surgical maneuver (Figure 51).

The use of SSEPs during opioid-based anesthesia is demonstrated in an example in a patient who had been given the opioid fentanyl and the neuroleptic agent dehydrobenzperidol (DHB). Following induction, there is a highly significant decrease in amplitude height and an increase in latency in the late peak (>100 ms) of the SSEP, suggesting sufficient analgesia. During the course of operation the analgesic wears off and with a sudden increase in nociceptive barrage amplitude height as the SSEP increases.

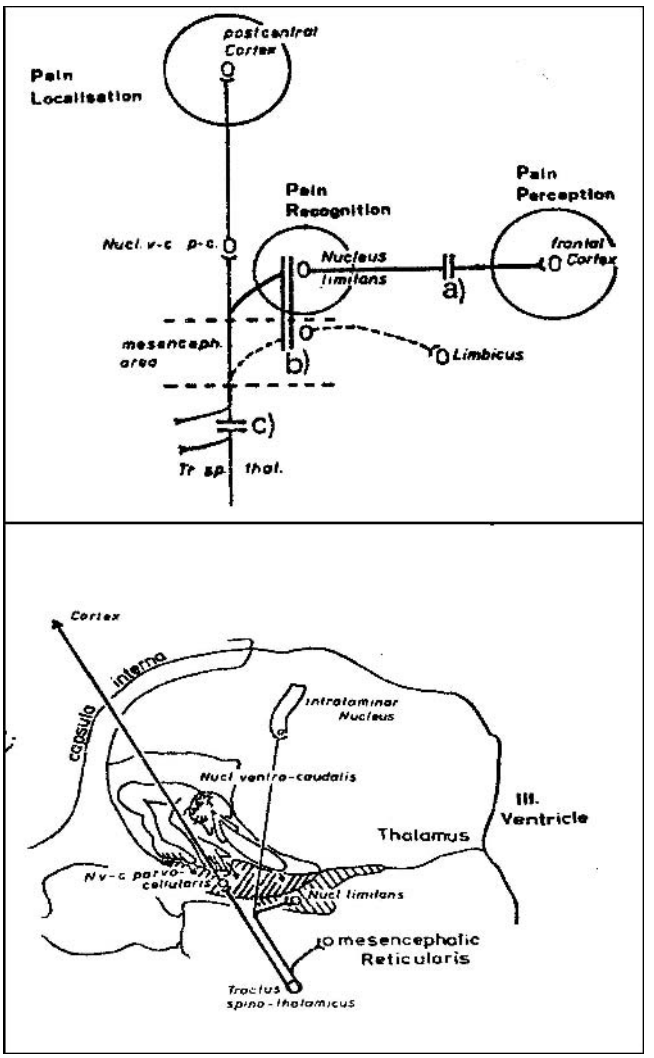


Fig. 49. The nucleus limitans, an important relay station in the mediation of nociceptive afferents to higher pain modulating and discriminating centers of the CNS, which is necessary for the nonspecific feeling of pain and is closely coupled with emotions. Adapted from [11].

This could rapidly be reversed by the additional injection of a low dose (40 μg/kg) of the short-acting yet powerful opioid alfentanil (Figure 52).

Use of somatosensory-evoked potential monitoring in the perioperative period

The following traces focus on the indications where SSEP monitoring has aided in intraoperative diagnostic finding and in critical care therapy. Most patients were monitored with the Lifescan^{TM} Evoked Potential Monitoring System using the following specifications:

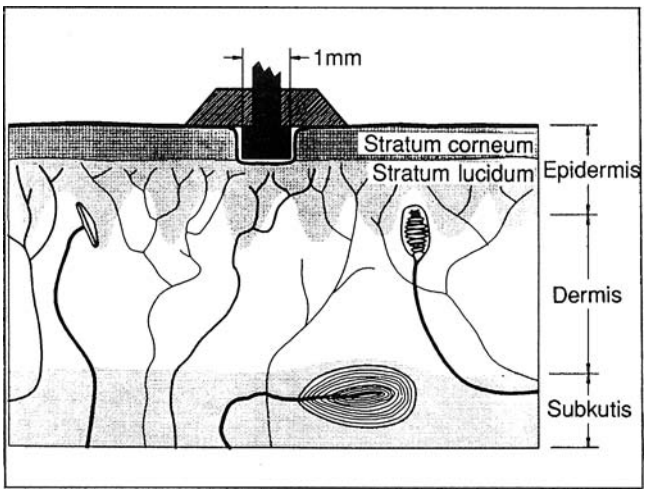


Fig. 50. Model for intracutaneous heat stimuli used for the evaluation of the analgesic efficacy different analgesic agents.

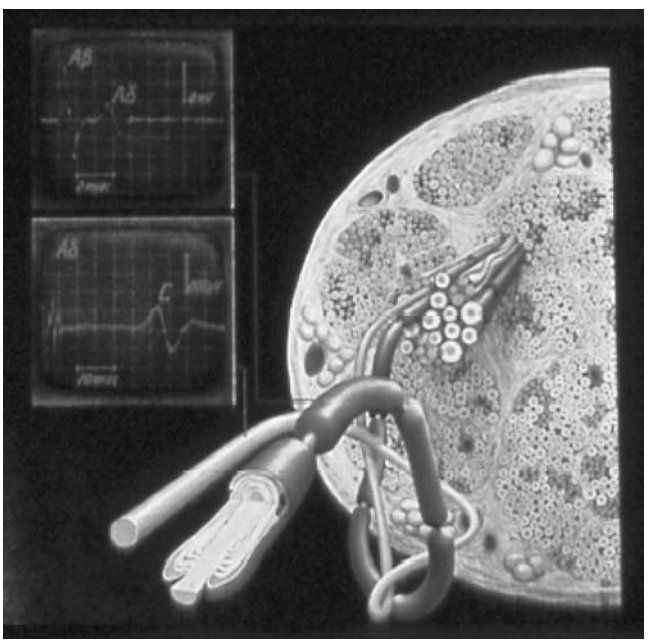


Fig. 51. Aδ- and C-fibers, which are activated during somatosensory evoked potential monitoring, using an electrical stimulus with 1 mA above motor threshold.

(a) Dynamic range 3–48 dB
(b) Window 30–1500 Hz
(c) Common mode rejection greater than 80 dB
(d) Filter setting is 120 Hz for a low-pass hardware filter and 0.2 Hz for high-pass hardware filter in addition using a 60/50 Hz digital notch software filter and a 30 Hz low-pass digital software filter
(e) Sampling rate 3.1 kHz/channel

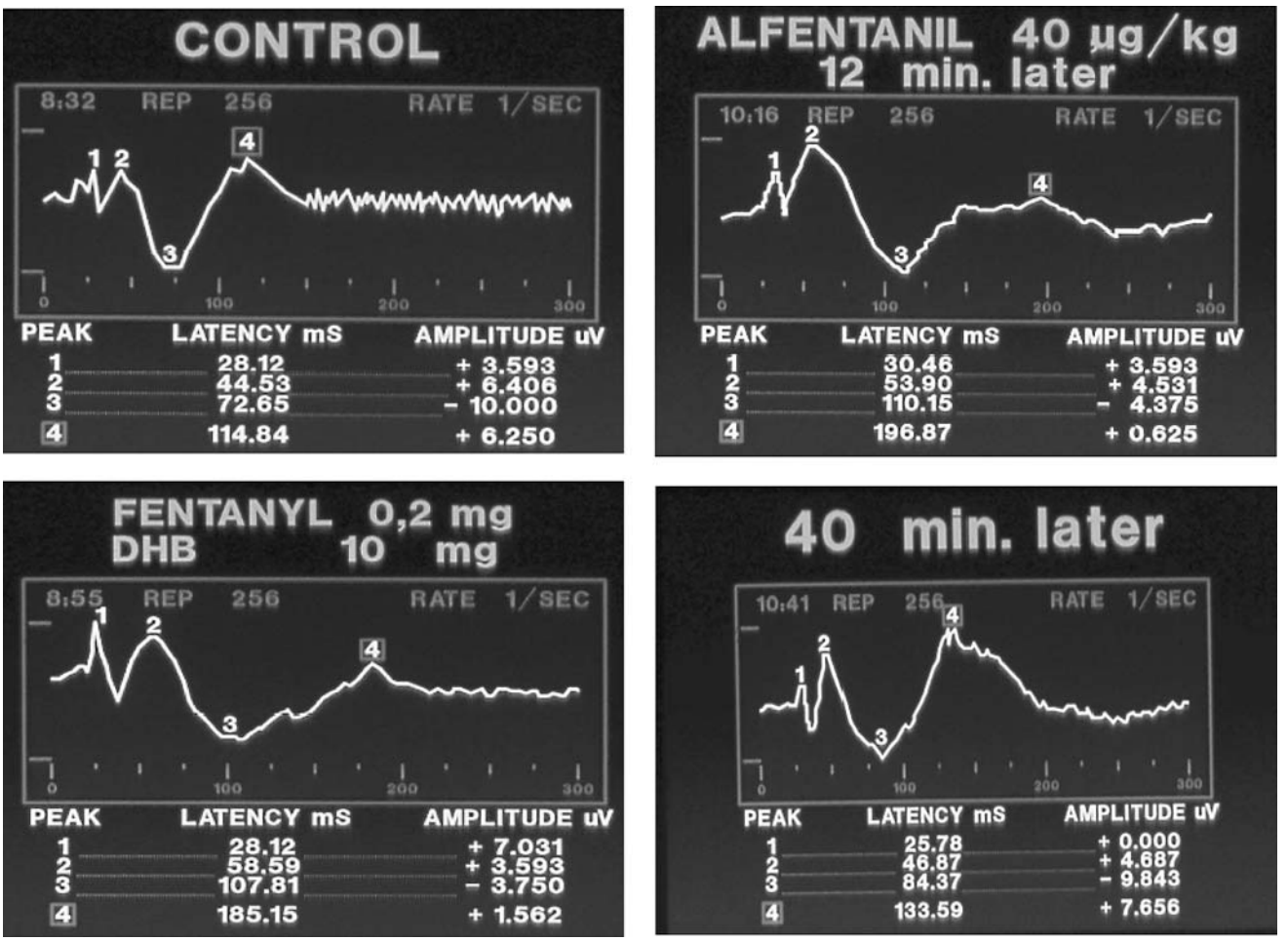


Fig. 52. Continuous median evoked potential monitoring in a patient with neuroleptanalgesia where the opioid fentanyl and the neuroleptic agent dehydrobenzperidol (DHB) are being administered. Due to an increase in nociceptive input, there is an increase in amplitude height of the late potential (peak 4). This effect is reversed by additional administration the short acting opioid alfentanil, an effect, which is terminated 40 min post injection.

Perioperative monitoring of somatosensory-evoked potentials

Induction with hexobarbital will result in a marked reduction of amplitude of the early but more so of the late (over 50 ms) peak when compared to the preoperative control period (Figure 53). This effect on the SEP suggests sufficient inhibition of nociceptive impulses, which may evolve following laryngoscopy for the insertion of the endotracheal tube. In comparison with the induction agent propofol, which has a pronounced hypnotic component, amplitude suppression is not that intense. The following intubation maneuver is not sufficiently blocked to prevent afferent volleys from inducing sympathetic discharge. This effect of propofol is due to paucity in analgesic activity and antitussive activity. The agent, however, induces a sufficient deep sleep stage.

During the course of anesthesia, evoked potentials are characterized by an increase in latency and a depression in amplitude height of the late peak of the SSEP (Figure 54). In general the early N_{20}-peak is little affected and only when nociceptive impulses are not blocked sufficiently there is an increase in amplitude height of the late peak ($>N_{100}$), which a significant sign to apply an opioid (Figure 54).

Postoperative recovery of sensory-evoked potentials

Evoked potentials monitored in a patient in the immediate postoperative period can be used for comparison with the preinduction period to evaluate whether the patient has sufficiently regained all his reflexes and there is no overhang

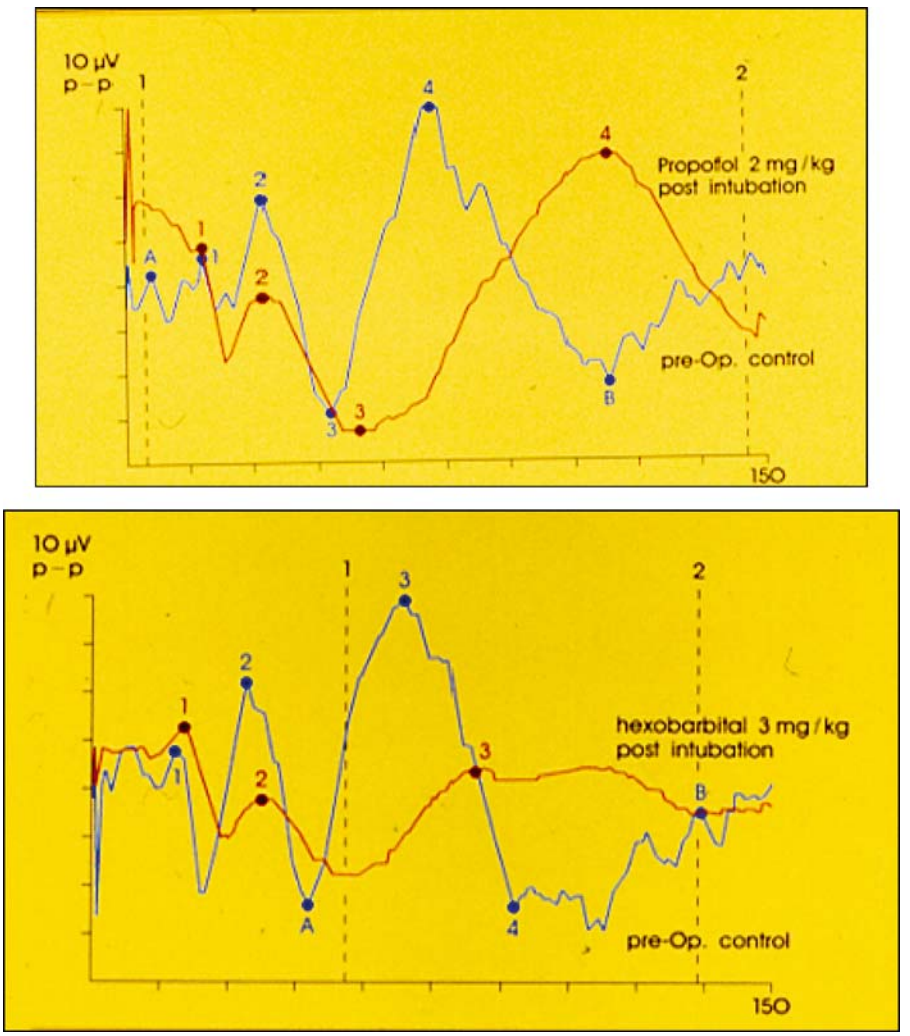


Fig. 53. Representative example of two agents used for the induction of anesthesia and their corresponding effects on median nerve somatosensory-evoked potential changes following laryngoscopy (time axis in ms). Top tracing propofol 2 mg/kg, bottom tracing hexobarbital 5 mg/kg.

of the anesthetic. But more so, SSEPs are useful to give an idea whether the impaired neurophysiological response suggests intraoperative brain damage. In the following figure the evoked potential, 20 min after the end of anesthesia, has a similar appearance as during the preoperative control period (Figure 55). Only the early peak (numbered 2) still is depressed in regard to amplitude height, reflecting a residual overhang of the anesthetic (enflurane N_2O/O_2-relaxant anesthesia).

A similar recovery is also observed following pure volatile anesthesia. Compared to the intraoperative period there is a reduction in the latency of the late peak and an increase in the amplitude height of the late potentials ($>N_{100}$; Figure 56).

Monitoring the depth of analgesia during anesthesia

During the anesthetic procedure SSEP are also helpful in determining the depth of analgesia. Although the patient may be sufficiently asleep, the SSEP monitoring suggests an insufficient blockade of nociceptive impulses to the higher subcortical pain-related centers. This reaction is earlier than the cardiovascular parameters (blood pressure, heart rate, lacrimation, movements) usually used in determining a sufficient level of anesthesia. While there a lag of up to several minutes in cardiovascular reactions, patients on AC-inhibitors, ß-blockers and other antihypertensive medications will not demonstrate any reaction. Therefore insufficient analgesia will go by unnoticed, resulting in the

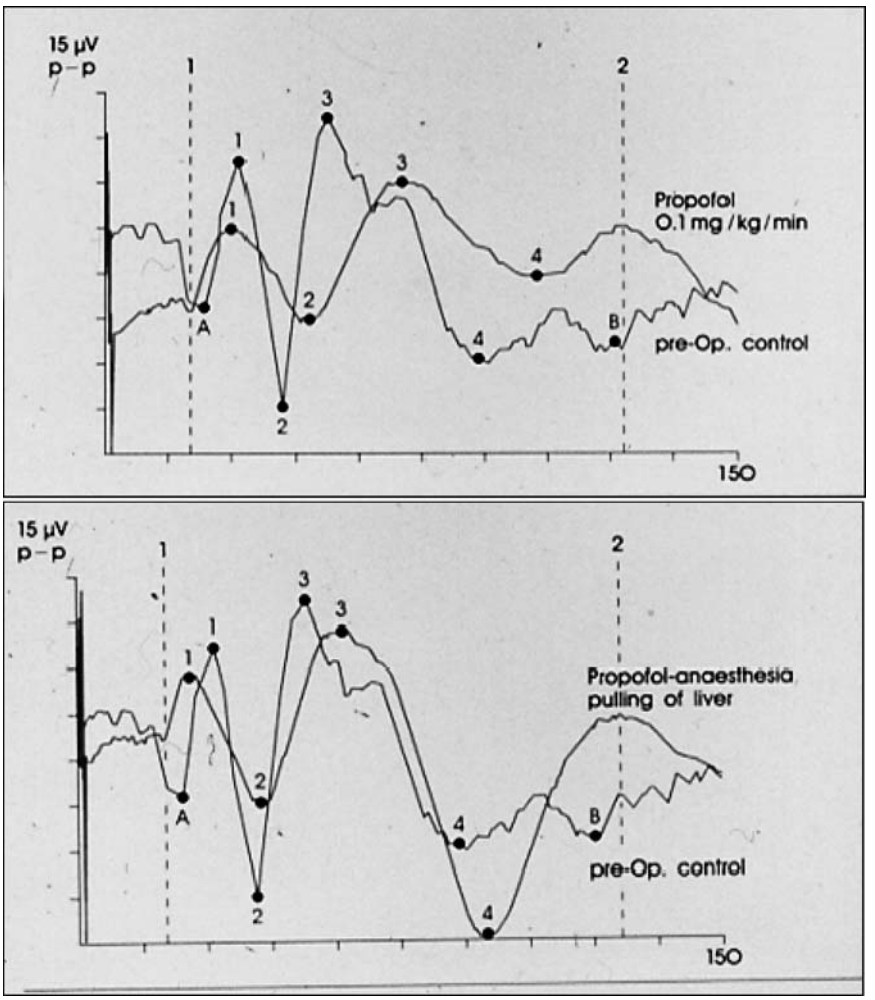


Fig. 54. Representative examples of SSEPs derived during the intraoperative period during steady-state propofol (0.1 mg/kg/min) N_2O/O_2-anesthesia, which is markedly changed by an increase in nociceptive input resulting an a tracing similar to that of the preoperative period.

possible sensitization of pain mediating centers in the spinal cord and pain modulating centers in the central nervous system. Since the goal of anesthesia is pre-emptive analgesia, which is not covered by a deep hypnotic stage, sufficient analgesia should individually be titrated by an opioid to the patient's need. A typical recording of a female patient (68 years of age) undergoing gall bladder removal is shown in the following figures (Figure 57).

Although the patient is sufficiently deeply anesthetized with propofol N_2O/O_2-relaxant anesthesia, the SSEP reflects an increase in amplitude and a reduction of latency during the time where the surgeon pulls at the liver. The peaks of the SEP are similar to the preinduction period and higher than at steady state anesthesia, suggesting insufficient analgesia. It was only after 3 min that blood pressure and heart rate, other indicators of insufficient anesthesia increased. This was corrected by the additional injection of a low dose (0.1 mg) of the opioid fentanyl.

A summary of evoked potentials derived during propofol- and enflurane-anesthesia with insufficient nociceptive blockade is depicted in the following figure. There the late peak (N_{100}) is used as a premonitory sign of analgesic depth where there is a significant increase of amplitude height, which is not significant between the two groups of patients (Figure 58).

Sufficient blockade of nociceptive impulses during the surgical manipulation is represented in another example during anesthesia with a volatile agent. Compared to the control-preoperative period (Figure 59), anesthesia with enflurane N_2O/O_2 at 1.5 vol% in a young male induces a suppression of the late (>50 ms) evoked peak.

During steady-state anesthesia the prior suppression of the late (>100 ms) peak of the SSEP is overridden when surgical manipulation induces an increase in nociceptive

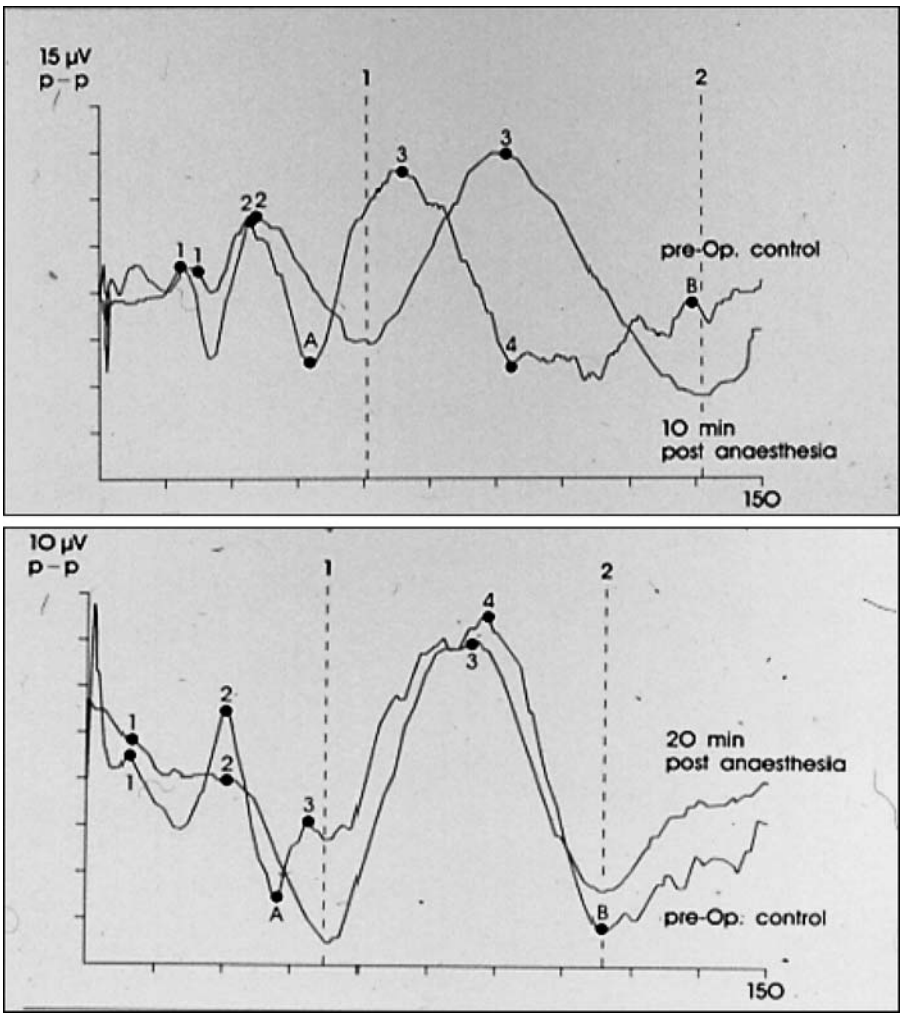


Fig. 55. Postoperative evaluation of the rapid recovery after following N_2O/O_2-anesthesia using evoked potential monitoring. Note: 20 min post anesthesia the peaks are practically identical to the ones taken preoperatively (time axis in ms).

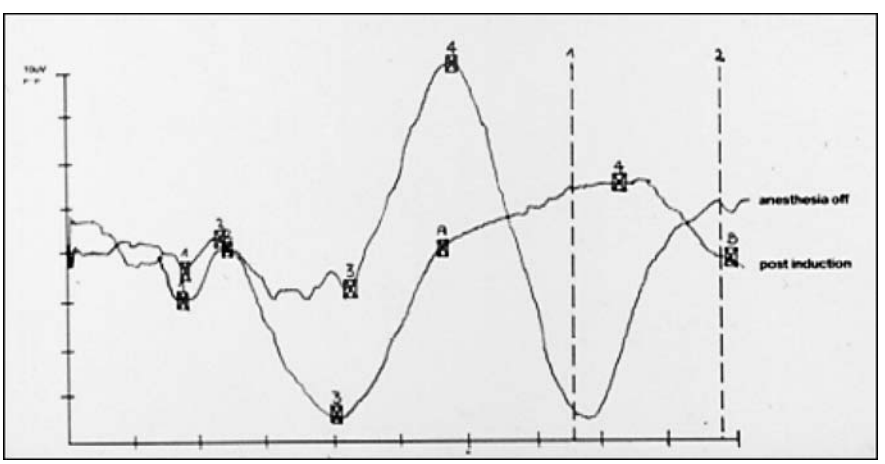


Fig. 56. Representative example after an enflurane N_2O/O_2-anesthesia where there is a recovery especially of the later peak in SSEP monitoring.

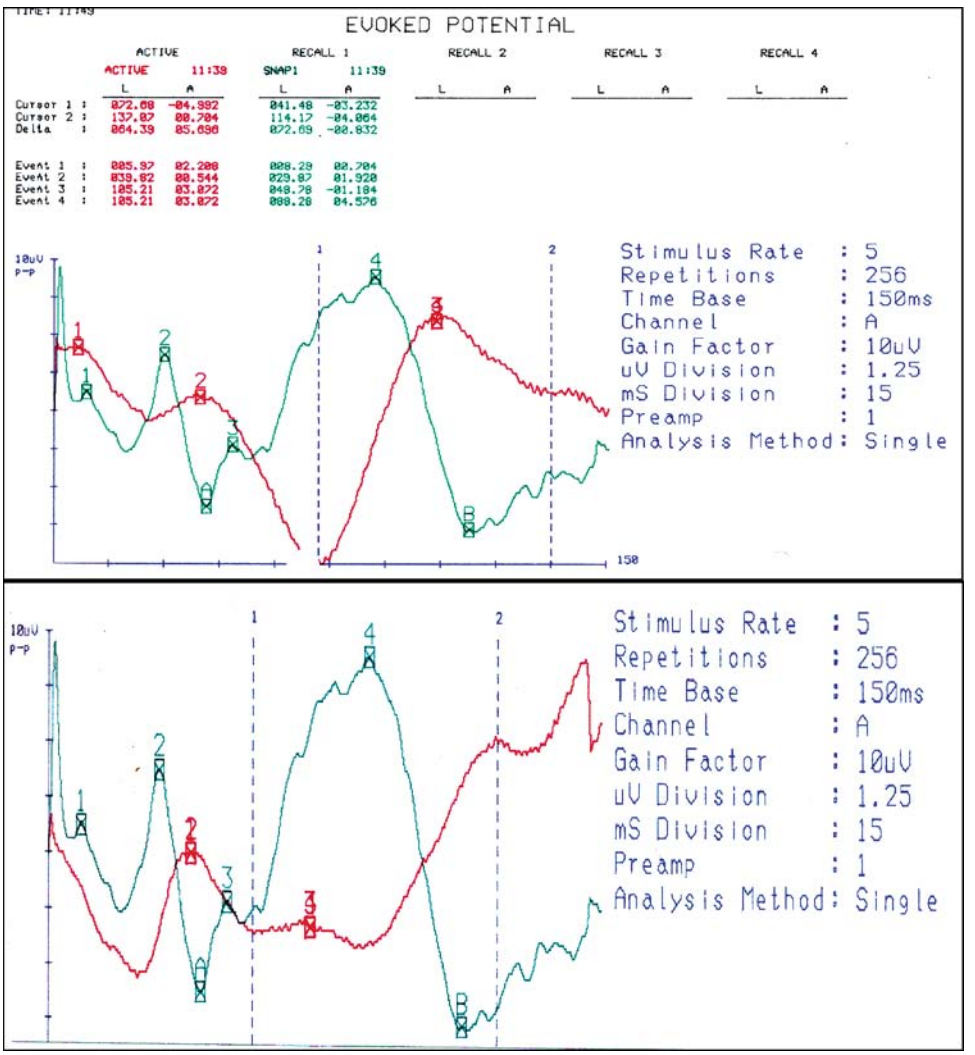


Fig. 57. Two representative examples compared to intraoperative SSEPs during propofol (0.1 mg/kg/min)-N_2O/O_2- anesthesia (red tracing) traction at the mesenterium (green tracing) results in an increase in amplitude and a reduction in latency reaching preanesthetic level (time axis in ms).

afferents, which results in an increase in amplitude height (bottom figure). This is followed by an increase in concentration of the volatile anesthetic to 2 Vol%. It is only after 5 min (when sufficient brain concentrations are reached) that the increase in afferent volleys within the somatosensory pathway is sufficiently inhibited in regard to nociceptive input and the generation of evoked potentials drops. Thus, the SSEP not only is useful to evaluate analgesia, as in experimental human algesimetry [20, 21], but the sensory-evoked potentials can give advance warning of insufficient analgesia during the operative procedure [18].

As mentioned earlier, the use of high-dose opioid anesthesia may result in a total loss of early as well as late evoked potentials. Such a situation, otherwise considered as a neurological deficit due to ischemia, is related to the anesthetic, which blocks all afferent volleys from crossing the synaptic cleft at the nerve junction (Figure 60).

Potent opioids thus induce an inhibition of nerve impulse afferents by selective blockade of receptor sites at the synapse. The following postjunctional deficit resembles the picture of a complete functional loss. This effect is related to the number of receptors in the somatosensory tract being occupied and can be completely reversed by the specific antagonist naloxone [10]. Also, the net effect of mixed narcotic analgesics such as nalbuphine can be evaluated in the human, using the SSEP as a method to determine analgesic effectiveness. In the following figure increasing doses of the analgesic result in a dose-related decrease of amplitude of the late (N_{100}) peak.

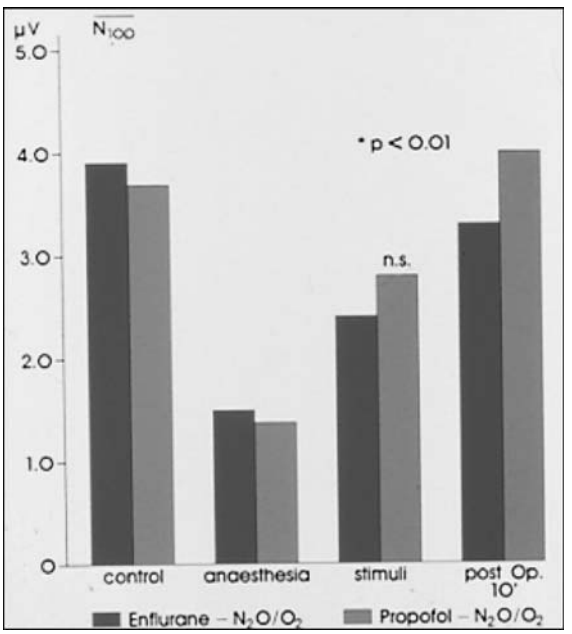


Fig. 58. Two groups of patients (each n = 10) receiving either enflurane or propofol-N_2O/O_2-anesthesia where the increased nociceptive input results in an increase of the amplitude height of the late N_{100} peak. Adapted from [17].

It can be seen that at 500 μg/kg a ceiling effect in regard to amplitude reduction is reached, as doubling of the dose leads to no further decrease of amplitude height. Thus, evoked potentials can be of use for testing in algesimetry when new compounds are evaluated in regard to their effectiveness and compared with other existing drugs (Figure 61). A similar use of evoked potentials has been described by others, who claim that late evoked potentials (>100 ms) correlate closely with the subject's individual feeling of pain sensation but not with stimulus intensities [18, 20, 21].

In conclusion, peaks with latencies between 30–70 ms (lower extremity) or between 13–30 ms (upper extremity) appear to be most stable for monitoring purposes during operation, as they are changed the least by volatile anesthetics. For monitoring of head injury or operations where the cerebral blood flow is at risk, such as during carotid endarterectomy or superficial temporal artery to middle cerebral artery bypass, the use of the central conduction time (CCT) from the cervical response (usually C2) to the sensory cortex is of considerable usefulness.

EVOKED POTENTIALS IN THE INTENSIVE CARE UNIT

In the ICU, serial analysis of cortical evoked potentials will give an idea of the possible status in patients with head trauma. A representative example shows a patient with severe head trauma who had been involved in a car accident. The SEP shows a marked difference in regard to right and left median nerve stimulation (Figure 62). Although CT scan revealed no signs of intracerebral mass bleeding, there was a left arm paralysis, a left sided mydriasis, with a radiological verified fracture at the base of the scull. The pathologically reduced amplitude of the early potentials during left median nerve stimulation suggested a left-sided functional deficit involving the medulla. In the following days of intensive care therapy, signs of recovery became evident as the amplitude increased in height being similar to right median nerve stimulation (Figure 62). Thus, the evoked potential was not only able to detect minute lesions in subcortical structures which otherwise are undetectable by CT scan, it also serves as a prognostic tool to evaluate the efficiency of therapy in the long run.

In addition, SSEPs can monitor the recovery in sedation when the patient has been given an opioid plus a benzodiazepine for tolerance of mechanical ventilation and for analgesia.

As demonstrated in Figure 63, tapering down the dose in sedation with an opioid and a benzodiazepine, there is a gradual recovery of the late peak in the SSEP. At the same time it can be seen that due to the long-time sedation regime, the overhang lasts up to 48 hours until the SSEP has fully recovered.

Somatosensory evoked potentials are also helpful when it comes to diagnose a potential peripheral nerve lesion after polytrauma. In a young female after a car accident with a fracture of the right forearm and head trauma, operative exploration of the peripheral nerve for decompression was considered necessary in order to avoid nerve lesion. While the comatose patient was on the ventilator and the right arm was in a cast, right median nerve stimulation revealed functional integrity with a sufficient evoked potential at Erbs point and no depressed amplitude of cortical evoked potentials (Figure 64). Thus, an otherwise unnecessary operation for the patient could be avoided. In the intensive care evoked potentials can give the clinician more information about the patient's central nervous function than any other monitoring system.

A 65 year old patient who had undergone aneurysm operation of the thoracic aorta, developed thrombosis of the vena cava, and meningitis arising from the ear postoperatively. He was in deep coma and an apallic syndrome was suspected. The EEG power spectra showed pathological slow delta to theta wave activity over both hemispheres. Median nerve evoked potential corroborated the diagnosis of cortical brain damage as only the early peak was derived while the late peak was practically flat. This suggested functional deficiency of cortical associative fields since the

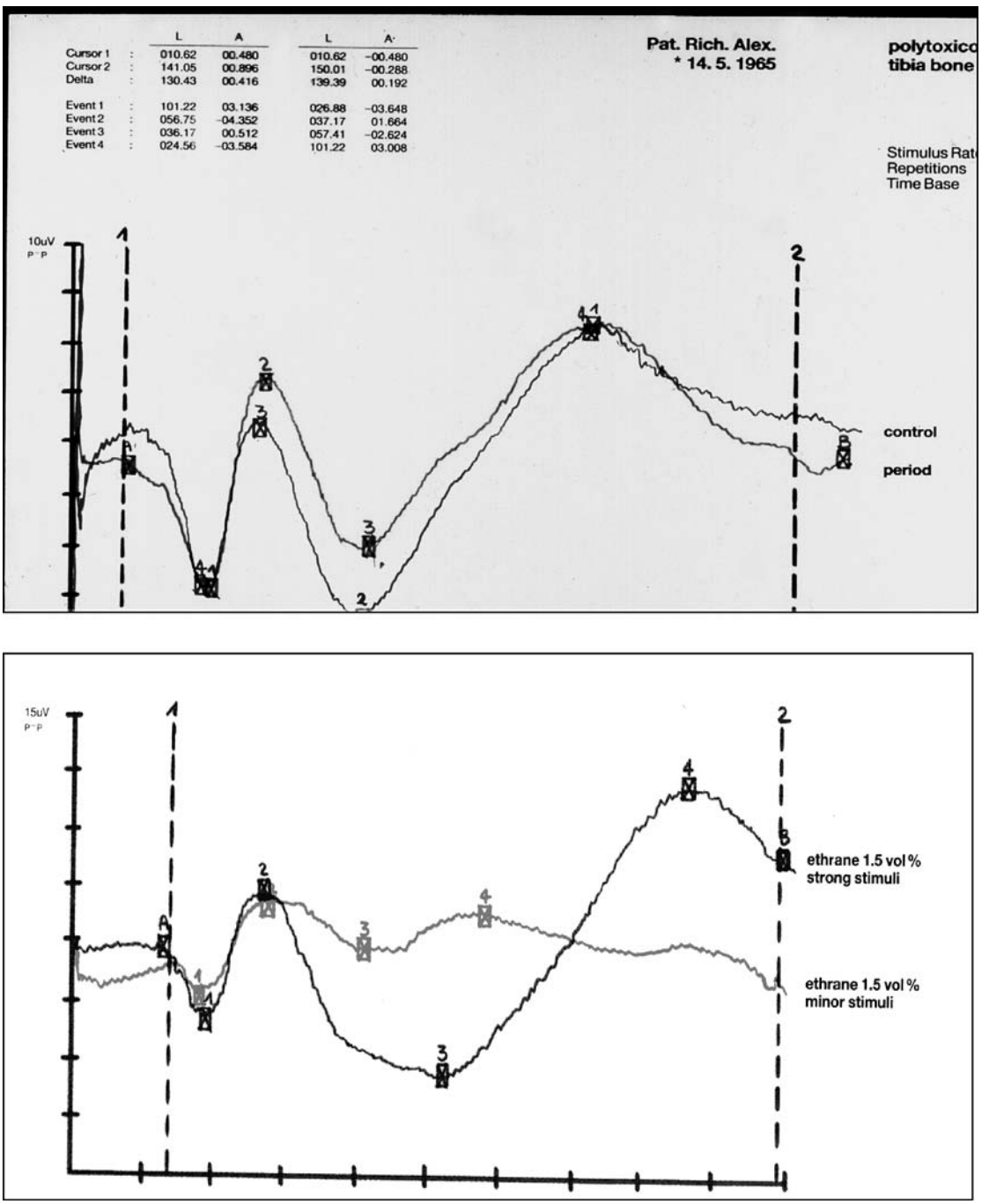


Fig. 59. Intraoperative monitoring of insufficient blockade of afferent nociceptive input using somatosensory evoked potentials in a young patient with polytoxicomania and tibia bone fracture. Compared to control (top) an increase in surgical stimuli results in an increase in amplitude height of the late peak (middle tracing) when major nociceptive input is induced by the surgeon. Insufficient analgesia is attenuated by an increase in the concentration (vol%) of the anesthetic enflurane (middle tracing), which however takes nearly 15 min until sufficient brain concentrations are reached (bottom tracing) X-axis = 15 ms/division; y-axis = 1.25 μV/division.

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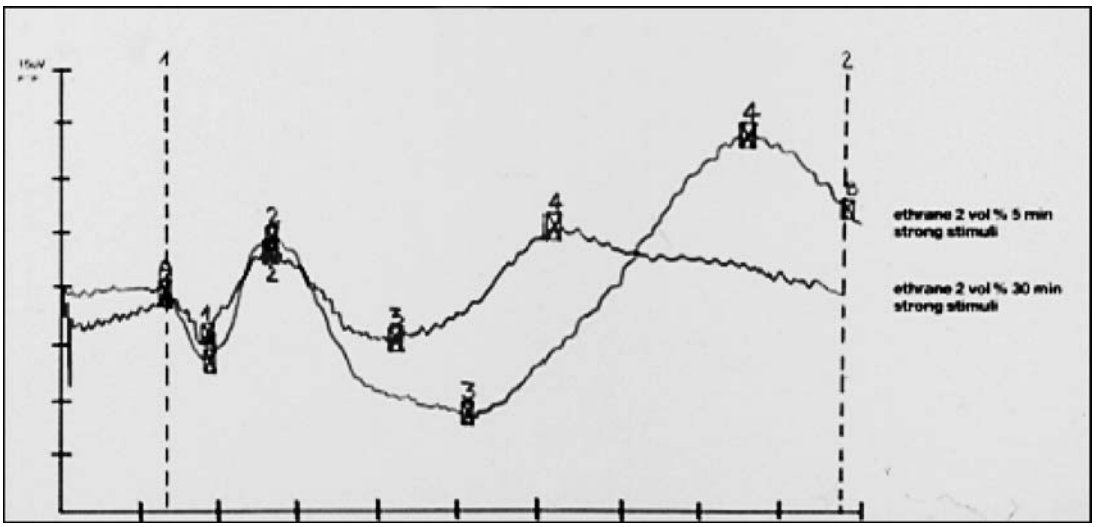


Fig. 59. (Continued)

patient had not received any sedatives or opioids over the past days (Figure 65).

Thus, the SEP is not only helpful in substantiating a suspected diagnosis; it can also be used to evaluate the efficacy of therapy and the possible prognostic outcome. It has to be noted that patients who are sent from the OR to the ICU for further supervision, often are in a hypothermic state which may effect SSEP monitoring. Especially in patients undergoing CABG (coronary aortic by-pass grafting), controlled hypothermia has a significant effect not only on peak latency changes, but also on the amplitude of the late peaks. This is reflected in an example of a 55-year-old male undergoing by-pass grafting. In comparison to normothermia with enflurane-N_2O/O_2 and fentanyl (Figure 66 green recording), deep hypothermia (22 °C) induced an increase in latency and a marked suppression of amplitude (Figure 66 red recording). This effect slowly reversed on rewarming. In the post bypass phase, normal temperatures resulted in similar evoked potentials as in the pre-by-pass phase.

Thus, hypothermia induces effects on the SSEP, which are similar to cerebral malperfusion. Therefore, it is always advisable to look at other parameters before making a final statement in regard to SSEP changes. And as demonstrated in the Figure 67, fentanyl in a dose of 0.35 mg has practically little effect on the early (<50 ms) evoked peak, which corroborates the results of other research groups [21]. Depression of CNS function during hypothermia, however, is reflected in the central conduction time (CCT). It shows the time lag of the evoked peak derived at Cz to the cortical peak N_{20} [23]. Cooling induces a synaptic delay of axonal conduction between wrist and cortex. During stable hypothermia, the CCT thus is a useful guide to monitor the cerebral status of the patient.

Sensory-evoked potentials in upper plexus and cervical root lesion

Besides evaluating central nervous functional pathways, the SSEPs can be helpful in the diagnosis of traumatic root lesion, for example of the brachial plexus. In such an incidence the functional deficit is in all parts of the corresponding nerve site while the contralateral side shows normal EPs. Thus, not only is the cortical EP flat, but also at Erbs point and at C7 no evoked potentials can be derived. A functional deficit in the area of the cervical root, i.e. rostral to the spinal ganglia, however, results in no change of amplitude and latency of the evoked potential recorded over the ipsilateral Erbs point. In those cases where the motor axons show partial degeneration, a slight amplitude reduction will be observed as the evoked potentials from Erbs point arises from mixed nerves in which the motor axons partly generate the potential.

If, however, the nervous pathways between Erbs point and cervical spine is affected by tumor infiltration, lesions of the cervical root by means of trauma, or local infection, peaks N_{11} and N_{13} are either reduced in amplitude or they are completely absent. These latter peaks are best visualized when the usual contralateral placed recording electrode has a contralateral shoulder as reference, or when the recording electrode over C7, Cz is taken as reference (Figure 68). In such instances, the potential at Erbs point has no deficit, as the point of obstruction is proximal to Erbs. According

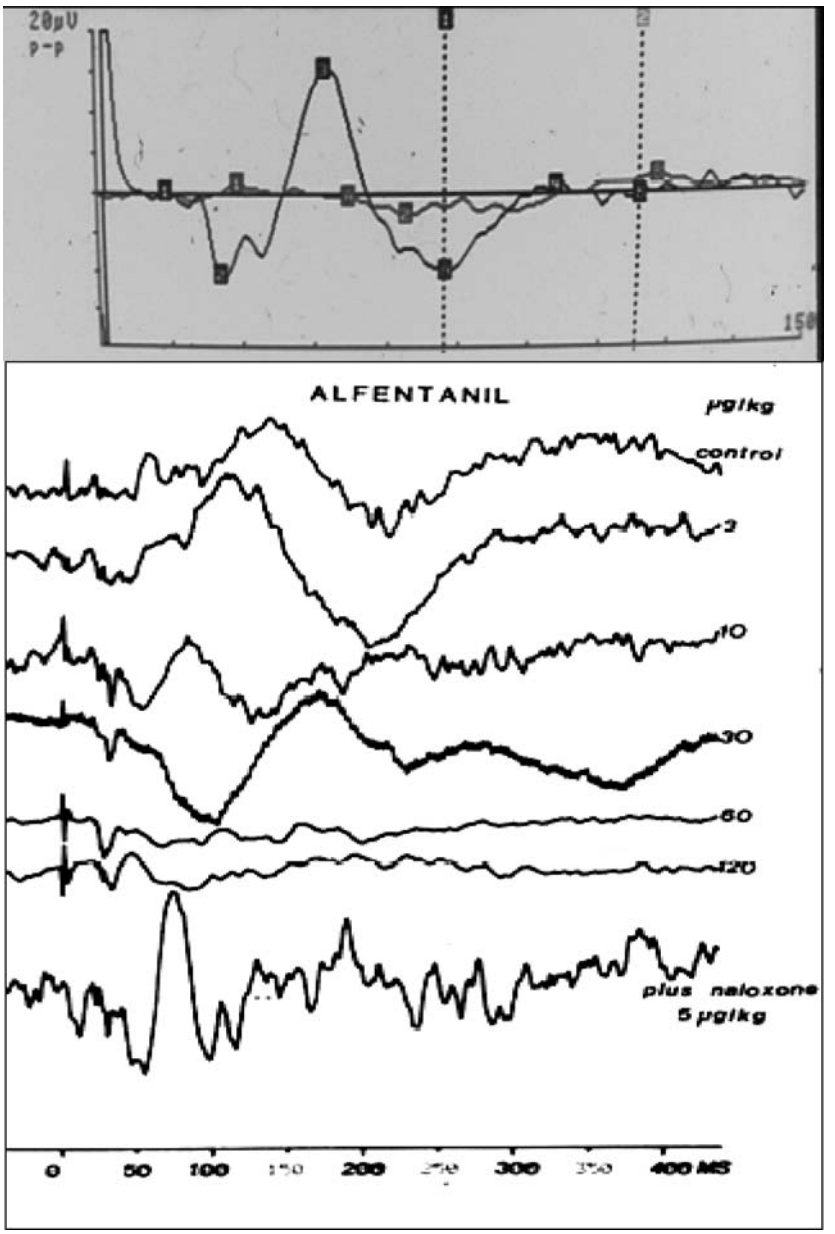


Fig. 60. Overlay somatosensory evoked potentials and increasing doses of the opioid fentanyl (50 µg/kg; top traces) and alfentanil (5–10–30–50–120 µg/kg; bottom traces) in the canine model. Due to complete receptor occupation there is loss of the cortical response. In the latter, this effect is reversed instantly by competitive displacement of the opioid by naloxone, the specific opioid antagonist.

to standard thinking N_9, N_{11} and N_{13} are generated in the brachial plexus, the posterior root of the spine, and the ascending afferent nervous tract respectively, while N_{14} is generated in the lemniscal tract [24–26] (Figure 69). However, it has to be underlined that all measurements have to be done on both sides in order to compare amplitude and latency changes. The N_{13} peak, as it is generated in the lower brain stem, is best visualized when the recording electrode is placed over the second spinal vertebra C2 (Figure 69).

Additionally, the electrode at position Cz is useful in determining the CCT (central conduction time) when the contralateral cortical evoked potential is recorded with a scalp electrode. The N_{13}/N_{20} transit time as well as the N_{20}/N_{13} amplitude quotient is also useful in the diagnosis of deficit in transit between the cervical spine and

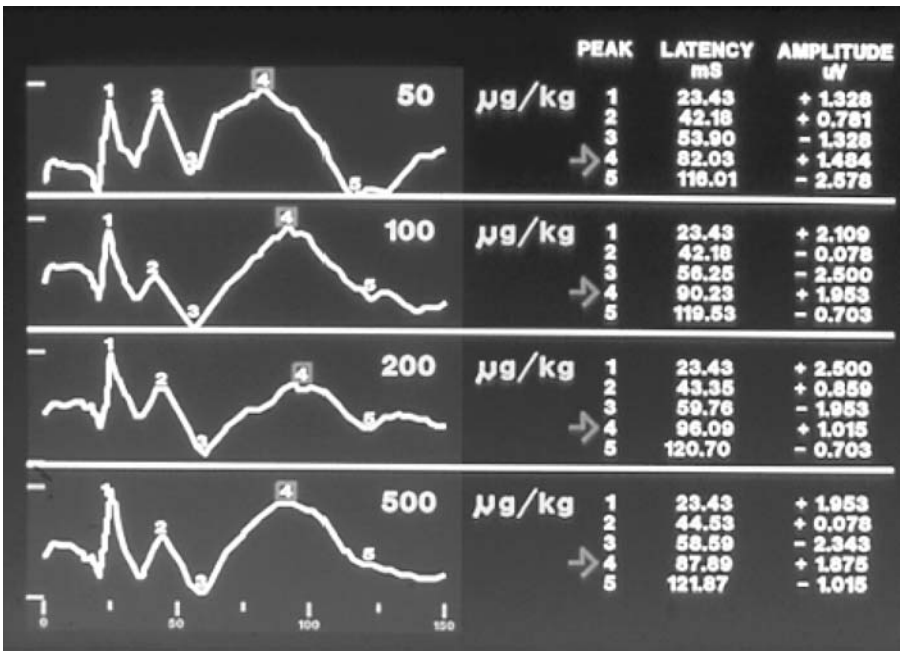


Fig. 61. The use of somatosensory evoked potentials in the evaluation of the analgesic effectiveness of nalbuphine postoperatively. Higher doses than 500 µg/kg result in a ceiling effect, i.e. the late N_{100} peak is not depressed any further (adapted from [19]).

the primary sensory cortex. A CCT above 7.25 ms and a quotient below 0.65 IμV can be considered pathological (Tables 10 and 11). From the above it is conceivable that a diagnosis can be derived using various quotients. Thus, any reduction in the C2/C7 value is an index for a functional deficit rostral to the cervical spine C7. The other quotient N_{20}/C2 reflects important information in regard to a partial deficit between the cervical spine and the pri-

Table 10. Normative values during median nerve stimulation. Adapted from [27]

Latency (ms)	Erb	C_7	C_2	N_{20}
Mean value ± SD	10.2 ± 0.9	13.5 ± 0.9	13.7 ± 0.9	19.3 ± 1.2
Upper limit (mean ± 2.5 SD)	12.4	15.8	15.9	22.3
Maximum right-left difference	0.7	0.7	0.7	1.1
Latency interval (ms)	Erb/C_2	Erb/C_3'; C_4'	C_7/C_2	C_2'; C_3'–C_4'
Mean interval ±SD	3.4 ± 0.6	9.0 ± 0.8	0.2 ± 0.2	5.8 ± 0.6
Maximum interval (mean ±2.5 SD)	4.9	11.0	0.6	7.3
Maximum right-left difference	0.6	0.7	0.6	1.0
Amplitude (μV) base to peak				
Mean value ± SD	3.7 ± 2.3	1.6 ± 0.7	1.6 ± 0.7	2.3 ± 1.0
Range	0.8–12.3	0.4–4.1	0.4–3.9	0.6–5.3
Side difference (%)	48	36	38	46
Amplitude quotient	Erb/C_7	C_2/C_7	C_3'; C_4'/C_7	
Mean	2.3	0.98	1.4	
Range	1.1–8.8	0.7–1.7	0.7–8.9	

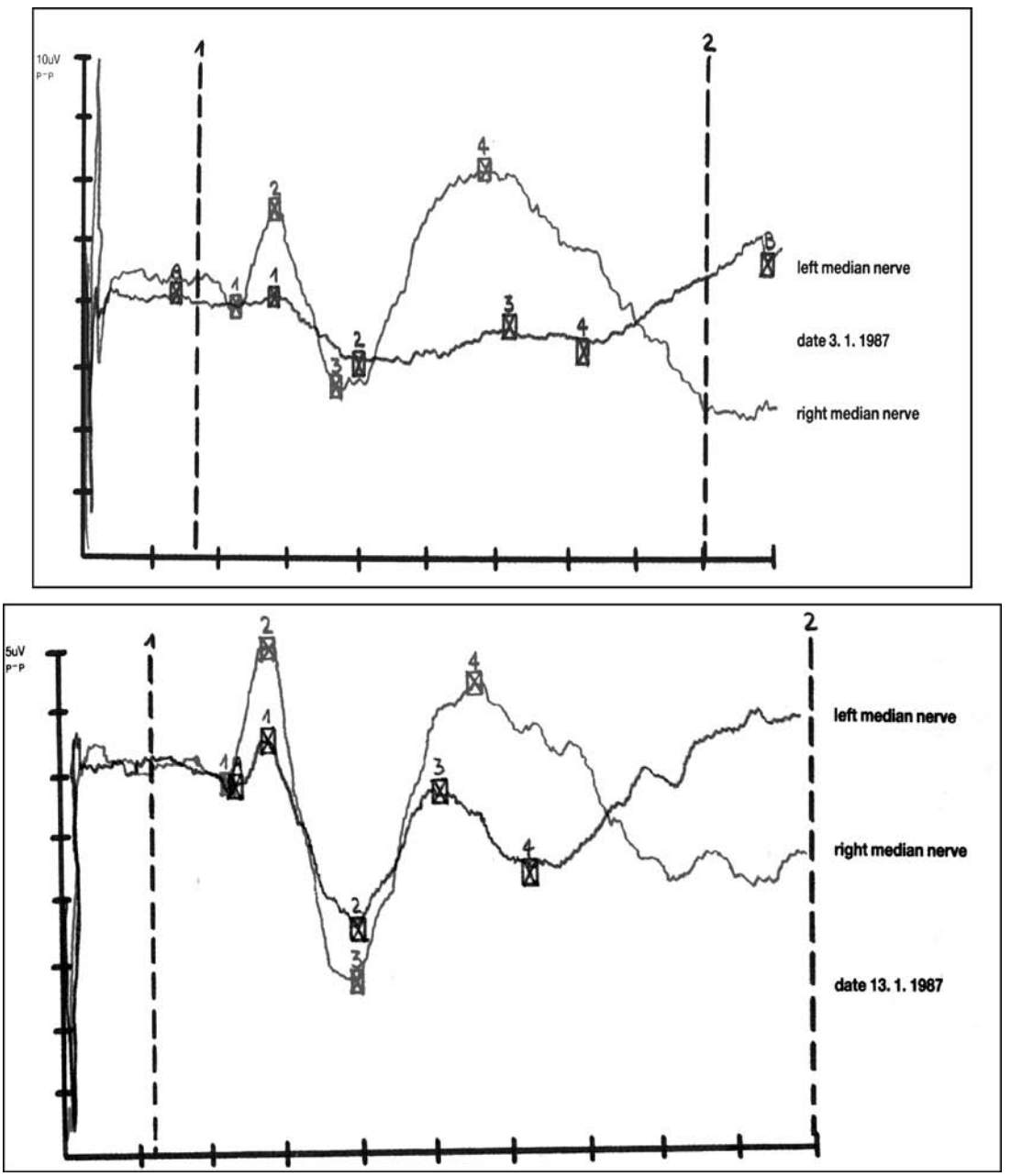


Fig. 62. Example of a comatose young male following severe head trauma where median nerve evoked potentials reflected side difference. During therapy in the ICU the suppressed amplitude at left median nerve stimulation recovers, suggesting functional improvement. The latter was also reflected in the patient's level of vigilance as he regained consciousness. x-axis = 5 ms/division; y-axis = 1.25 μV/division.

mary sensory cortex, especially when the value drops below 0.65 μV.

Involvement of the medulla by trauma, degeneration or by infiltration of a tumor, results in changes of the SEP with the recording (active) electrode over C2 during median nerve stimulation. In such an instance, the usually well definable N_{13} peak is deformed while cortical recording depends on the extent of the affection, followed by a deformation of amplitude and reduction as well as an increase in latency.

The locked-in-syndrome, which is due to an infarct in the pontine area, results in a total deficit of voluntary

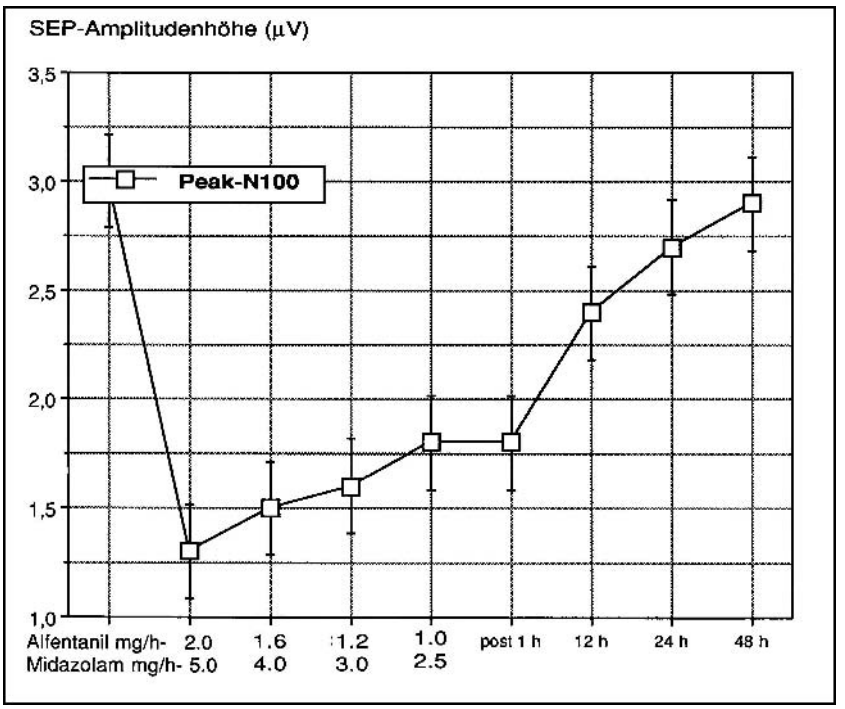


Fig. 63. Change of the late peak of the SSEP using different doses of alfentanil/midazolam in 10 patients undergoing sedation in the ICU. Adapted from [22].

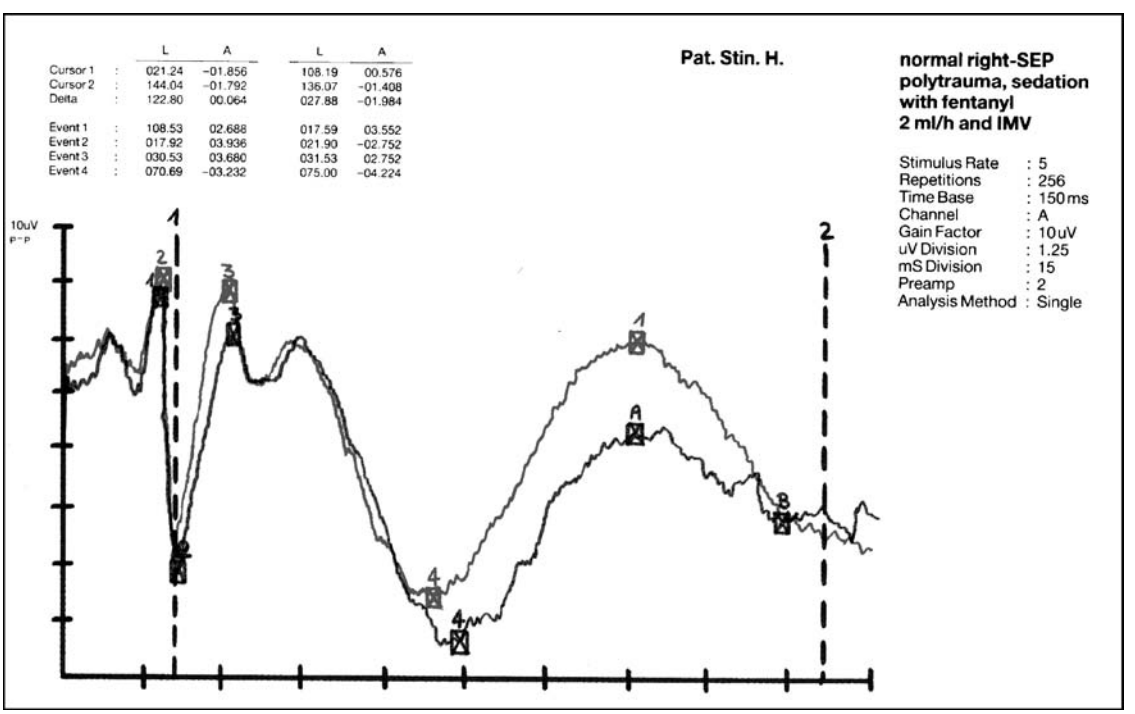


Fig. 64. Right median nerve evoked potentials derived in a comatose young female with questionable peripheral right arm nerve compression. The normal SEP suggests functional integrity.

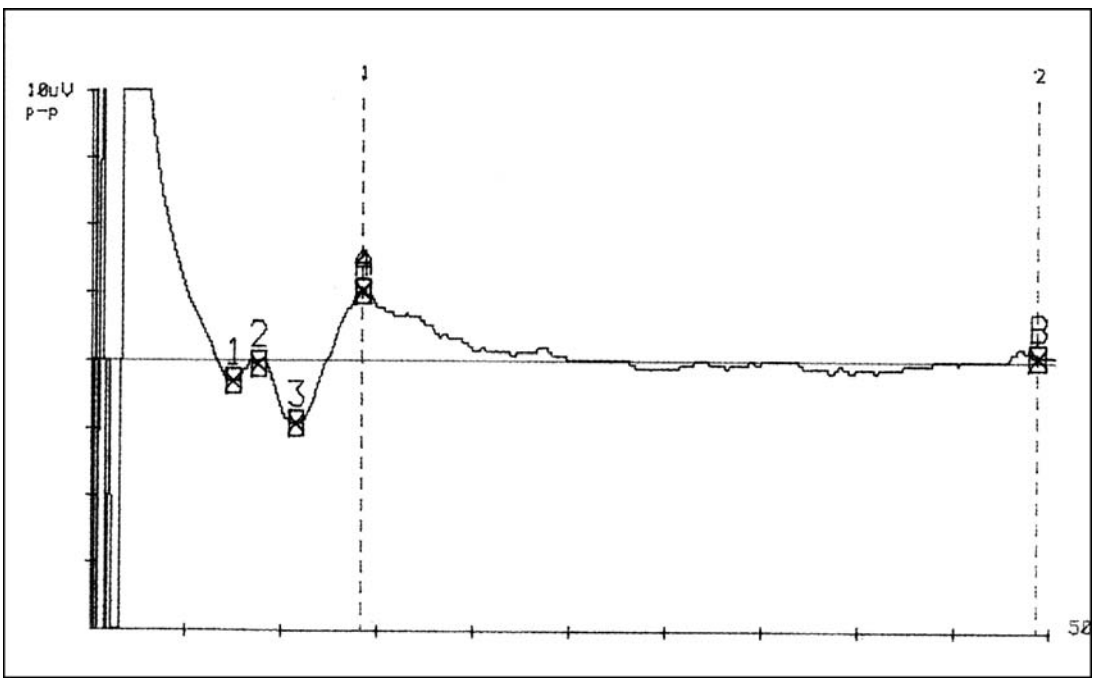


Fig. 65. Posttraumatic deep coma in a patient with pathological delta activity in the EEG powers spectra. In the SSEP only the early peak is derived suggesting cortical lesion.

movements with the exception of vertical eye movements. The SSEP in such a case is characterized by a total loss of early as well as late cortical EPs with a N_{13} peak clearly visible over the cervical spine C2. Any reduction in the amplitude by at least 40%, when compared to the other side, is a clear index of pathology, which is characteristic in the locked-in-syndrome, as well as in posttraumatic deficits due to bleeding in the thalamus (Figure 70).

Table 11. Normative values during posterior tibial nerve stimulation. Adapted from [28]

Latency (ms)	N_{18}	N_{22}	N_{30}	P_{40}
Mean value ± SD	18.4 ± 1.2	21.7 ± 1.6	29.5 ± 1.9	38.8 ± 2.0
Upper limit (mean ±2.5 SD)	21.4	15.8	34.3	43.9
Latency interval (ms)	N_{18}/N_{22}	N_{22}/N_{30}	N_{30}/P_{40}	N_{22}/P_{40}
Mean interval ± SD	3.8 ± 0.9	7.9 ± 1.0	8.8 ± 1.6	17 ± 1.7
Maximum interval (mean ±2.5 SD)	6.0	10.4	12.9	21.3
Maximum right-left difference	2.66	2.41	2.81	3.5
Amplitude (μV) base to peak				
Mean value ± SD	0.3 ± 0.2	0.6 ± 0.3	0.6 ± 0.3	1.8 ± 1.3
Range	0.05–0.8	0.15–1.1	0.15–1.25	0.35–5.2
Maximum side difference (mean ±2.5 SD)	0.51	0.5	0.54	2.5
Amplitude quotient	N_{22}/N_{18}		P_{40}/N_{22}	
Mean	3		4.9	
Range	1.1–6.6		0.85–27.3	

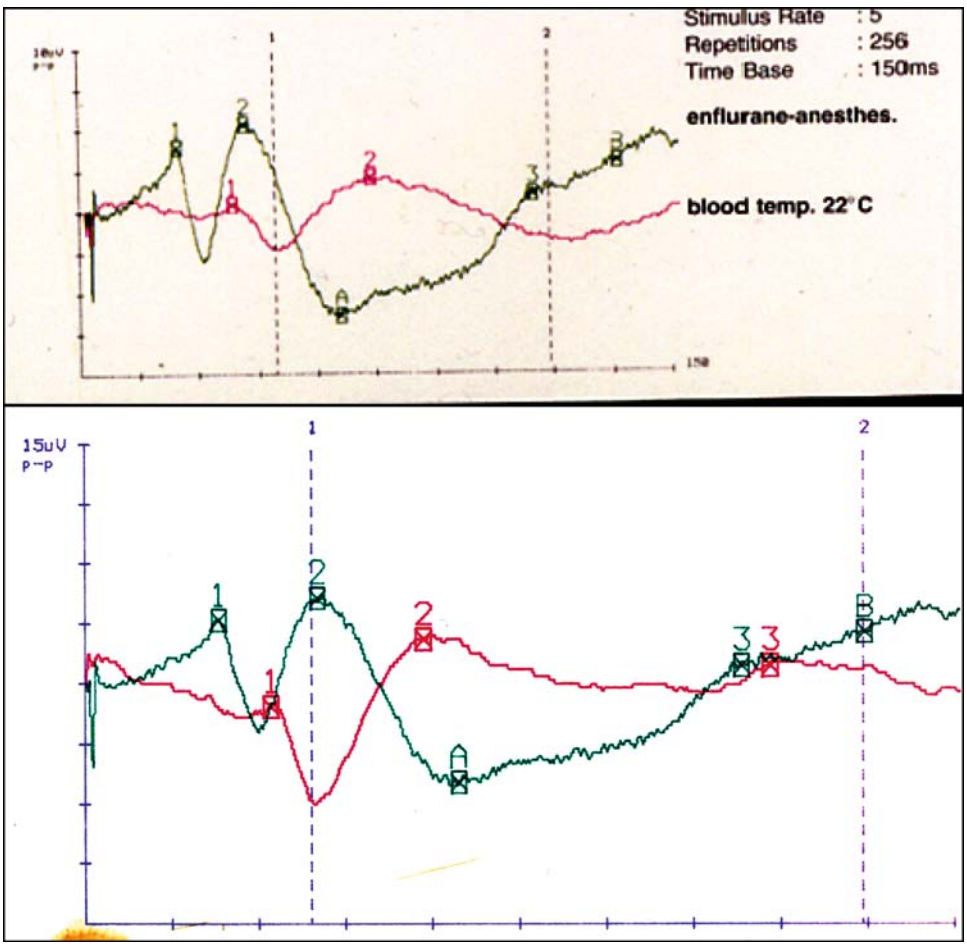


Fig. 66. The effect of cooling on median nerve SSEPs in patients undergoing CABG during bypass. Hypothermia induces latency changes and amplitude depression similar to the effects of malperfusion.

If the infarcted or traumatized area is localized posterior to the postcentral gyrus a normal N_{20} peak, the primary complex, will result even though the late peaks are completely missing. Such a picture can be interpreted as presence of functional integrity of the postcentral gyrus. Any lesion that extends from the cortex down to the capsula interna will result in a total loss of all cortical components. In certain cases it is advisable not to take FpZ as the point of reference, but to choose instead the ipsilateral shoulder as reference and C_3' or C2 as the active electrode. Once FpZ and C_3' have similar negative polarities, it is conceivable that in an electrode montage FpZ-C_3' the resultant potential will be zero (Figure 71).

Use of SSEP in head trauma, vascular disease, and brain death

Of clinical use in the intensive care unit are SSEPs when a barbiturate therapy in traumatic coma, used for the protection of the brain blunts the usual clinical methods of diagnosis. In addition to the usual indications of SSEP measurements in head trauma, this diagnostic tool is of prognostic value. Besides measuring the cervical (C7, C2) and cortical evoked potentials during median nerve stimulation, the interpeak latencies $C2/N_{20}$, also referred to as the central conduction time (CCT), as well as the interrelation of the amplitudes N_{20}/N_{13}, can be useful parameters. Similar to the usual neurologic evaluation, the non-traumatized side serves as comparison. Abnormal or slightly prolonged CCT and normative or only slightly diminished ratio amplitude reflects a good prognosis. A marked prolongation of CCT, however, and especially an amplitude reduction of cortical responses in addition to the low amplitude quotient N_{20}/N_{13} strongly suggest a poor outcome. Any bilateral loss of the cortical response can be considered of bad prognostic value. In the diagnosis of cerebral death, the SSEPs, even in the case of bilateral loss of cortical responses, up untill now are not considered to be a definite

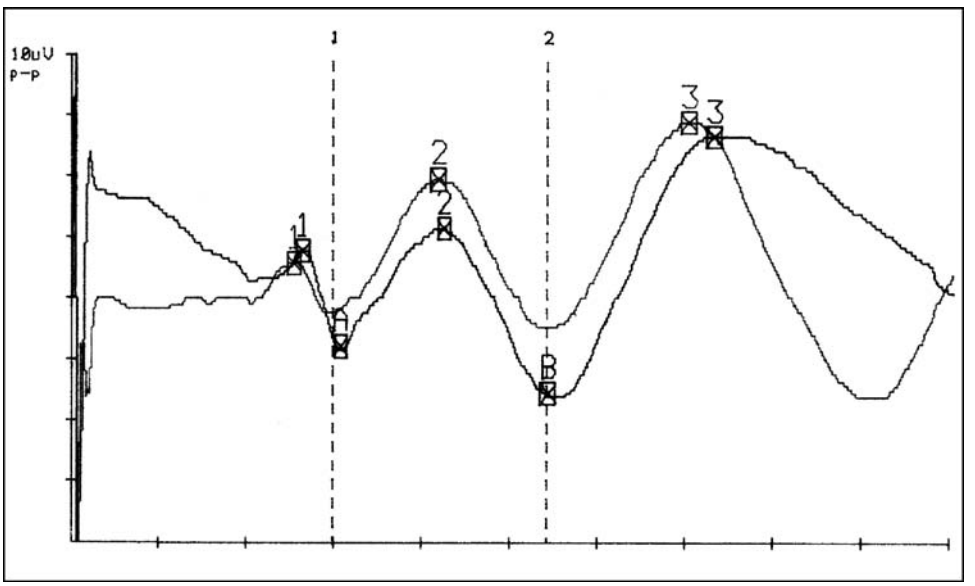


Fig. 67. Representative example of median nerve early evoked potentials using the montage C_3'-F_3; tracing 5 ms/division, sweeps 1012, Peak 1 = N_{13}, Peak 2 = N_{20}, Peak 3 = N_{35}.

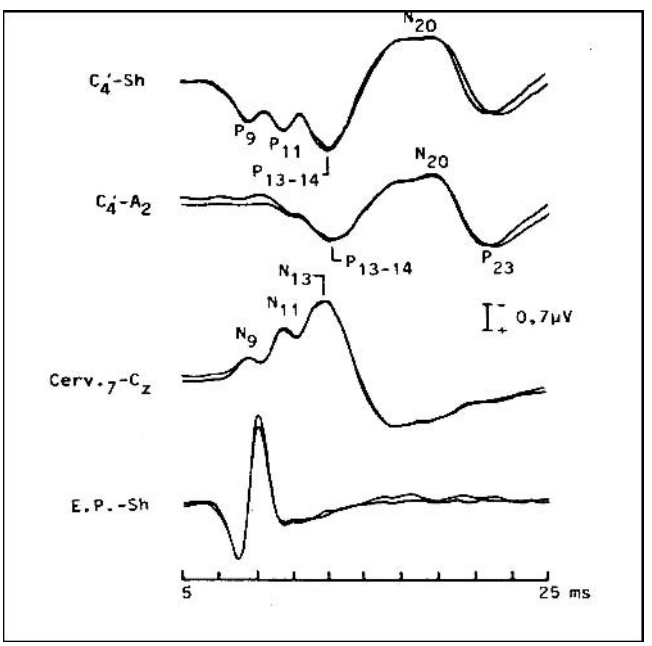


Fig. 68. Short latency evoked potentials during median nerve stimulation using different reference sites; EP = Erbs point; Sh = Shoulder; A_2 = Right ear lobe.

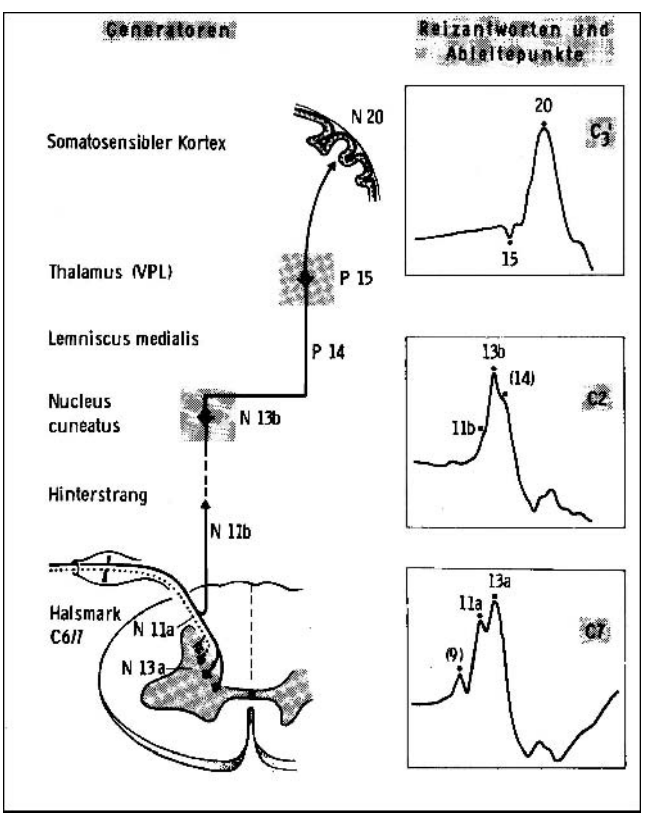


Fig. 69. The generators of spinal and cortical SSEPs during median nerve stimulation.

sign of permanent brain death. Such a diagnosis can be reached with the aid of early acoustic-evoked potentials (AEPs). This is derived from the fact that any irreversible loss of brain stem activity is a prerequisite of cerebral death.

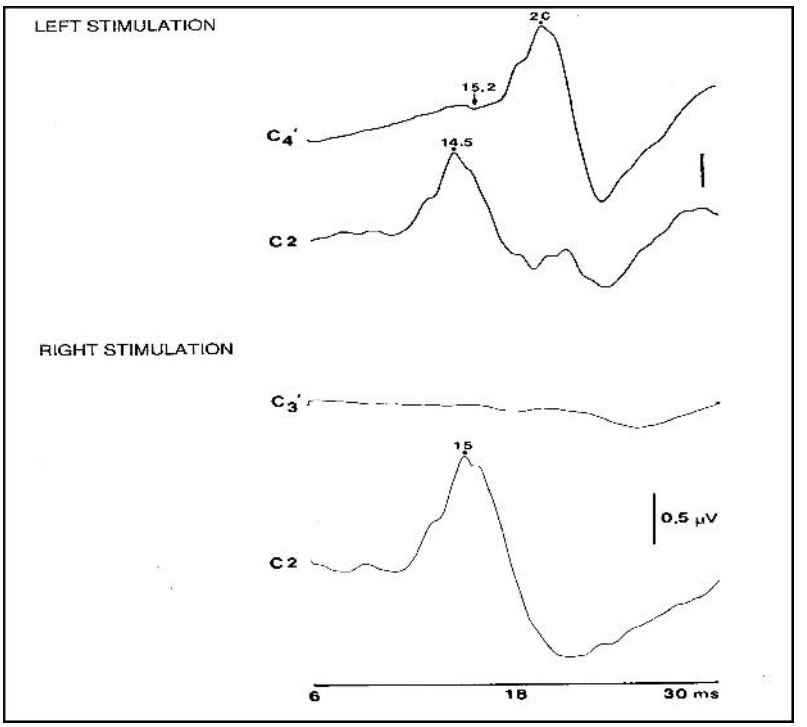


Fig. 70. Left-sided intrathalamic bleeding and the corresponding median SSEP. Adapted from [29]).

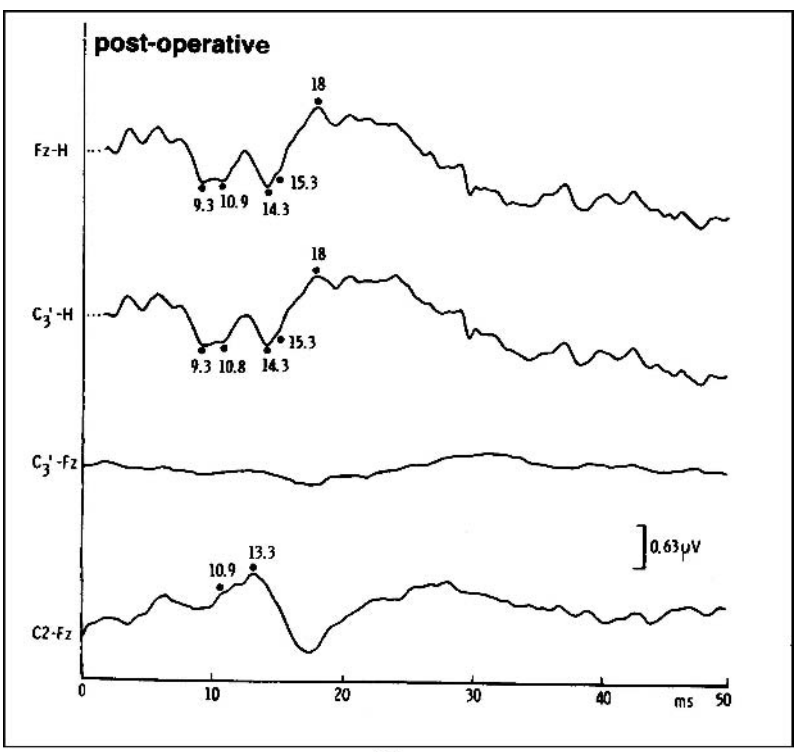


Fig. 71. SSEP recording following neurosurgical operation. At C_3'-FpZ position no potential can be derived. If, however, the hand or the shoulder is taken as reference, a peak can be derived. This is due to the similar polarities at C_3' and FpZ.

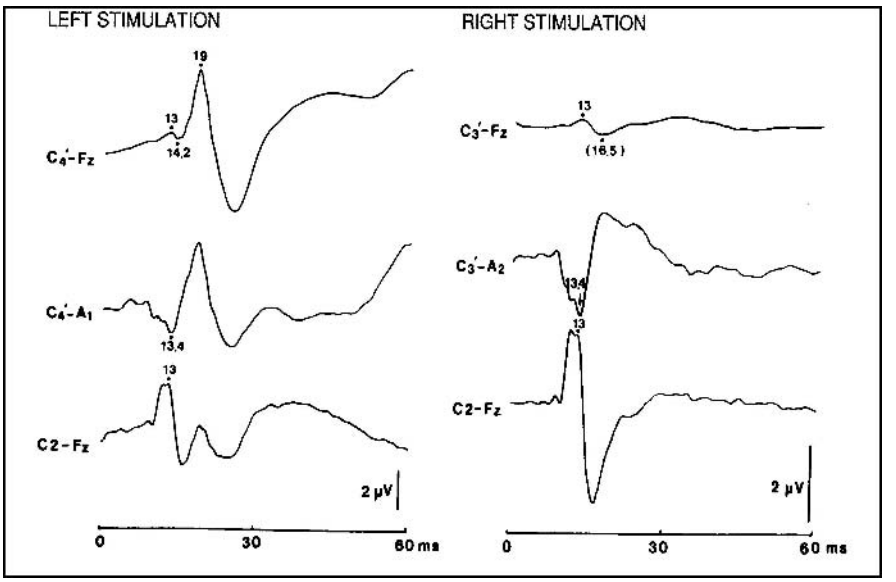


Fig. 72. CT scan verified infarct of the cerebral media artery and its effect on the median SEP. The late peaks over the left hemisphere are missing.

However, in addition to the bilateral loss of cortical evoked potentials during SEP measurements the peak derived from C2 (the N_{13} peak) can be considered a useful sign of an intact medulla as this peak is generated in the lower part of the brain stem. Brain death can thus also be diagnosed with the SSEP, especially when the active electrode over C2 detects no peak. Any primary loss of that potential after head injury is a sign for a combination of cortical and lower brain stem involvement. In vascular attacks such as an infarct of the middle cerebral artery the early phase in the SSEP is characterized by a marked distorted shape with amplitude suppression, which is related to the area of hypoxemia [30]. SSEP diagnosis in this regard can be used as an aid to control the course of the ailment (Figure 72). Also, in transitory ischemic attacks the increase of latency in the SSEP can be used to monitor the functional deficit of the underperfused area [31]. Similar to cortical evoked potentials, being a diagnostic tool during cerebral hypoxemia, hypoxic phases of the spinal cord may also be detected, as they appear for instance during aortic cross-clamping of an abdominal aneurysm. Spinal cord ischemia very soon after aortic clamping is characterized by a marked depression of amplitude, which finally may result in a total loss of any signal ascending to the cortical level. As different protective techniques are fostered to increase survival time of the spinal cord, SSEPs are used as a tool to evaluate any residual hypoxic effect after declamping [32]. An alternative way to monitor spinal cord function during aortic surgery is the recording of the evoked potential from the scalp produced by epidural stimulation at L3/L4 (also see chapter on Spinal Cord Monitoring). Spinal cord potential disappearance with tibialis stimulation often is not caused by ischemia of the lumbar spinal cord, but by ischemia of the peripheral nerve. Such monitoring during aortic cross clamping is the only way of early detection of ischemia which otherwise is masked by anesthesia.

From the above and in accord with the literature [33, 34], the usefulness of SSEP monitoring during vascular and open-heart surgery can be summarized as follows:

1. Any increase of CCT above 20% with a depression of amplitude of the N_{14} and N_{20} peak during carotid clamping which after declamping will not resolve, is bound to end with a neurological deficit.
2. Any drop of mean pressure during ECC (extracorporeal circulation), accompanied by a reduction of amplitude in the order of 20–50%, is a monitoring sign of insufficient perfusion and should be followed by an increase of perfusion pressure.
3. In aneurysm clipping of the common cerebral artery, the SSEPs derived during posterior tibial nerve stimulations are likely to pick up any deterioration in blood distribution. Specific changes of the early N_{20} or P_{26} peak can be seen. Thus, a time axis of 50 ms is sufficient for evaluation. Clipping of the so-called Pica aneurysms should be done under continuous monitoring of SSEPs in order to evaluate borderline perfusion and pick up insufficient blood supply to cerebral areas.
4. In aneurysm clipping of the anterior cerebral artery, malperfusion is best diagnosed during posterior tibial

nerve stimulation. Any increase in CCT signaling malperfusion in this pathology, cannot be considered a reliable sign.
5. Hypoxic effects during aneurysm clipping of the posterior cerebral artery are monitored best when the active electrode is positioned at P_3 or P_4 rather than at position Cz.

In any case, with the aid of SSEPs, the cerebrovascular reserve can be monitored directly during the clipping procedure before permanent damage will evolve. In spite of the potential advantages SEP monitoring in the OR and/or the ICU may bring, it should be remembered that the evoked potential is only a warning signal of malfunction of the specific pathway in the nervous system. Potential drawbacks of this methodology are:

1. It takes time for the averaging procedure, and depending on the number of sweeps, it sometimes will take up to 3 min.
2. Only the afferent pathway in regard to its function is monitored, not the efferent pathway.
3. The SEP is not a diagnostic instrument to tell the physician about the cause of the underlying malfunction.
4. Neuromonitoring after head trauma will only be able to diagnose a functional deficit. Usually there is a good correlation of CT and SSEP. In some cases, however, the SSEP is a better diagnostic system, as the former will only evaluate changes in morphology. If density difference is below 8 mm, the CT is unable to visualize these changes.
5. Normal SSEPs provide no direct evidence of intact motor function, as the major parts of the CNS tested during SEP monitoring are the dorsal columns of the spinal cord. In acute spinal trauma and during operations involving the spine, fortunately sensory and motor function usually corresponds closely [27].
6. Irreversible carotid occlusion can be associated with postoperative SEP deficit in the monitoring pathway. However, when obliteration is reversed, the resulting waveforms will return to normal before the end of anesthesia signaling a preservation of function.
7. The central conduction time (CCT) of SSEPs has a close correlation to the prognostic outcome in comatose patients.

In special circumstances such as identification of the central sulcus, the monitoring physician should prepare the patient for a median nerve SSEP and record a scalp cortical response after induction of anaesthesia but prior to surgical preparation, to determine if a response exists. If, as a result of the underlying pathology, the response is absent or there is very low amplitude, subsequent cortical surface recording may be difficult. Once the cortex has been exposed, the surgeon places a sterile subdural electrode strip containing at least four electrodes across the suspected central sulcus. Responses are recorded using a common reference on the scalp ipsilateral to the stimulated side, using either a surface or subdermal needle electrode applied prior to draping. A polarity reversal occurs across the central sulcus following median nerve stimulation at the wrist. If position is precentral, the response is initially positive (P_{20}), and postcentral it is initially negative (N_{20}). Once the central sulcus is identified the surgeon can better avoid working near the sensorimotor cortex, which will minimize postoperative neurological deficits.

For dorsal root entry zone identification this requires direct stimulation of, and recording from, the spinal cord. The purpose of this surgical procedure is to electrically ablate an area of the dorsal root entry zone (DREZ) of the spinal cord that is presumed to be generating pain signals that cannot be controlled (Figure 73).

A complication of this procedure is extending ablation too far laterally, thus affecting the dorsolateral tract fibers and leg motor function. Since visual identification of the exposed DREZ during surgery may be impossible in cases of long-standing complete root avulsion, spinal cord conduction techniques are used to precisely identify the DREZ. Briefly, the rostral end of the exposed cord is stimulated with very low current (0.2–0.5 mA) at the known dorsolateral tract, and a silver ball electrode records the spinal cord evoked response from the caudal, exposed cord using a subdermal needle reference electrode in the wound. The baseline response amplitude should be no greater than 20 μV. The stimulating electrode is then moved to the dorsal column tract and a second recording is made. The dorsal column response is smaller and slower for the same stimulus intensity. Stimulation at the DREZ results in no response because longitudinal tracts do not exist at this point. This identifies the DREZ.

PITFALLS AND POINTERS FOR SSEP MEASUREMENT IN THE OR AND THE ICU

Anesthesia: Avoid inhalation agents when monitoring intermediate or long-latency evoked potentials. Obtain pre-anesthesia base-line recording. Avoid bolus injection of CNS active drugs during monitoring periods.

Circulation: Monitor intra-arterial pressure. Avoid fluctuation of perfusion pressure during critical phases of measurement.

Electrodes: Use silver/silver chloride or gold electrodes. Attach electrodes with collodion. Protect electrodes with tape or gauze. If used within the surgical field, platinum subdermal electrodes should be used.

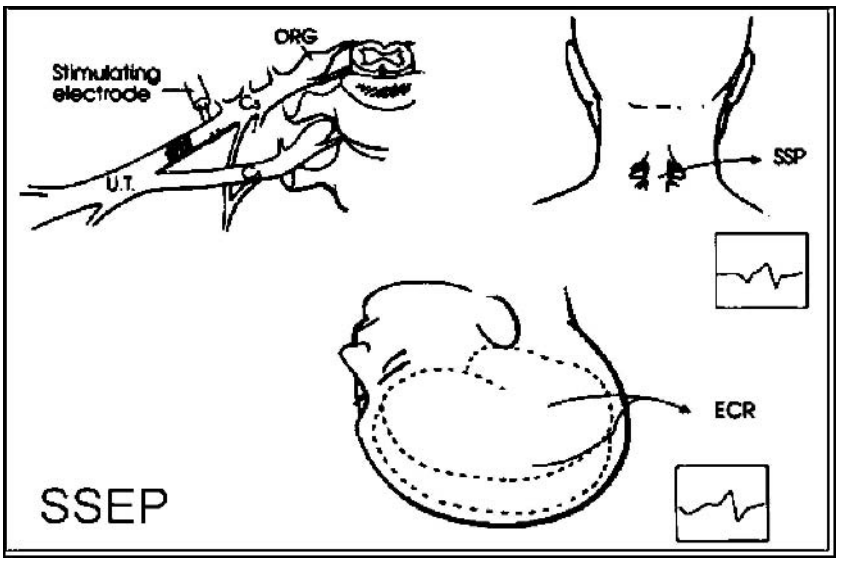


Fig. 73. Identification of dorsal root entry zone (DREZ) in SSEPs.

Muscle relaxants: Somatosensory stimulus should be supra-threshold prior to the administration of a muscle relaxant.

Noisy recording: Electrode impedance should be less than 3 kΩ and matched. If in doubt, inspect the raw EEG for artifacts. Protect the electrodes under surgical drapes. Twist electrode lead wires together. Suspend recording during electrocautery.

Respiratory gases and ventilation: Keep anesthetic concentration and $paCO_2$ constant during phases of measurement.

Technique: Meticulous recording technique is more important in the OR and the ICU than in the EEG laboratory.

Temperature: Maintain stable temperature of stimulated extremities by wrapping them up in blankets.

SUMMARY FOR SSEP MONITORING DURING THE PERIOPERATIVE PERIOD

Somatosensory evoked potentials (SSEPs) are monitored during surgery with two primary goals in mind:

(a) To monitor the function of neural structures at risk of iatrogenic injury, and
(b) To identify specific neural structures.

Neuromonitoring may be useful during surgery that may affect spinal cord function (deformity correction, traumatic spinal fracture repair, tethered cord release, spinal cord mass removal), brainstem function (posterior fossa mass removal), brain function (carotid endarterectomy, aneurysm repair), and peripheral nerve function (pelvic fracture surgery). Neuroidentification may be useful during surgery for removal of cerebral masses near the sensorimotor cortex (central sulcus identification or cortical mapping) and ablation of spinal dorsal root entry zone (DREZ) for pain relief (identification of DREZ and adjacent spinal tracts).

SUMMARY OF PRINCIPLES IN NEUROMONITORING

Neuromonitoring using SSEPs requires:

(a) Stimulation of a site caudal to the neural structure at risk, and
(b) Recording of evoked responses in at least one site caudal, and one site rostral, to the neural structure at risk.

The caudal site will monitor the effectiveness of the stimulus, while the rostral site will monitor the passage of the evoked response through the neural structure at risk. A diminished rostral response during surgery, in view of a maintained caudal response, leads the monitoring technologist to look for possible technical reasons for the change and, if none are found, informing the surgical team of the change. This can allow surgeons to alter the surgical procedure in an effort to alleviate a dysfunction if possible. Technical reasons for a change in the rostral response include increases in anesthetic agents or medication bolus, displacement of recording electrodes, increased electrical noise.

1. For stimulation electrodes either surface electrodes or subdermal needle electrodes can be used. Due to constant impedance, needle electrodes can deliver a more consistent stimulus in long cases. Although rare, electrical burns from stray capacitances have occurred when using subdermal needle electrodes. Prevention is based on a well-applied ground electrode and caution when electrocautery is in use, i.e. separate the electrocautery leads from the neuromonitoring leads.
2. The stimulus is of rectangular type, with biphasic pulses using either constant current or constant voltage, duration of 100 to 200 msec, and an intensity about 1.5 times above motor threshold. Intensity should not exceed 20 mA or 60 V for subdermal electrodes, and 50 mA or 150 V for surface electrodes. Since large cortical responses are obtained at low stimulation rates, optimal suggested rates for cortical recordings are between 2 and 5 per second that are not evenly divisible into the line frequency (for example, 1.3/s). Higher rates, up to 20/s, can be used for subcortical monitoring because subcortical responses are less affected by higher stimulation rates than cortical responses.
3. For median nerve stimulation, the cathode should be placed about 4 cm proximal to the distal wrist crease between the tendons of the palmaris longus and flexor carpi radialis muscles; the anode should be placed 2–3 cm distal to the cathode. For ulnar nerve stimulation, the cathode should be placed about 4 cm proximal to the distal wrist crease on either side of the tendon of the flexor carpi ulnaris muscle, and the anode should be placed 2–3 cm distal to the cathode. For posterior tibial nerve stimulation the cathode should be placed between the medial malleolus of the ankle and the Achilles tendon just proximal to the malleolus, and the anode should be placed 2–3 cm distal to the cathode. For peroneal nerve stimulation, the cathode should be placed in the lateral popliteal fossa just medial to the tendons for the biceps femoris muscles, and the anode should be placed 2–3 cm distal to the cathode.
4. Both sides should be monitored independently and, if the equipment is able, responses from both sides should be displayed on the same screen by alternating left and right stimuli with a short delay between them. The analysis time (sweep length) for upper limbs is 50–75 ms per limb, and for lower limbs, 100–125 ms per limb. If cortical response amplitudes are insufficient to begin with, synchronous bilateral stimulation will result in a larger cortical response allowing monitoring to proceed. With bilateral stimulation, however, it is possible to miss unilateral SSEP deterioration. If only one stimulator is available, responses must be recorded independently in an alternating fashion.

For registration/recording, the monitoring physician should endeavor to optimally record evoked responses with respect to time, amplitude, and stability. An evoked response change is easier to interpret when starting with a large, stable response that can be recorded quickly. The following parameters are intended to provide an optimally large, stable response:

The suggested *general bandpass* of 30–1 kHz is relatively narrow to provide a stable response. If the initial cortical response is too small for neuromonitoring, the low-frequency filter can be lowered. If spinal potentials have an unstable baseline, the low-frequency filter may be raised to 100 Hz. The *gain* should be set at 100,000 or a sensitivity of 10 to 20 μV/division, while the display gain can be adjusted to optimally display the waveforms (about 0.5–10 μV/division). If noise is activating the automatic reject function, the next less sensitive gain may be used. For *electrodes*, subdermal needle or surface electrodes can be used for recording. Needle electrodes are convenient due to their ease of application. Surface electrodes applied using collodion and conductive gel are less invasive and carry a smaller risk of electrical burn because of the larger surface area contacting the skin.

For upper limb SSEPs, a *4-channel montage* is suggested:

Channel 1 with electrode montage at EP-left and EP-right, channel 2 with electrode montage at C2-Fpz, channel 3 with electrode montage at C_3'-FpZ, and channel 4 with an electrode montage at C_4'-FpZ. An alternating montage is channel 1 at C_3' or C_4' to Fz, channel 2 at C_3' or C_4' to Erbs point contralateral to the scalp, channel 3 at Erbs point ipsilateral to the side of stimulation to Fz, and channel 4 at C2 to Fz. Also, a two-channel system can be effective using channel 1with an electrode montage at EP left-EP right and channel 2 with electrode montage at C_3'-C_4' with reference to Erbs point, which is generally located just above the clavicle and just lateral to the insertion of the sternocleidomastoid muscle. C2 is the second level of the cervical spine. This site can be placed roughly in the midline of the upper, posterior neck. C_3' and C_4' are 2 cm posterior to C_3 and C_4 of the International 10/20 System for electrode placement (Figure 74).

For posterior tibial nerve stimulation, the following montages are suggested including channel 1 with left popliteal fossa (PF) – medial knee, channel 2 with right popliteal fossa (PF) – medial knee, channel 3 with C2-Fpz, and channel 4 at Cz′-Fpz (or C3′ to C4′).

An *alternating montage* is channel 1 at Cz′-Fpz′, channel 2 at C3′ or Cz′-Fpz′ (or C3′ to C4′), channel 3 at interspinous ligament or epidural space to reference electrode (R) on the spinous process at the same level proximal to the surgical site, while channel 4 is at the interspinous ligament or epidural space caudal to reference. The caudal electrode

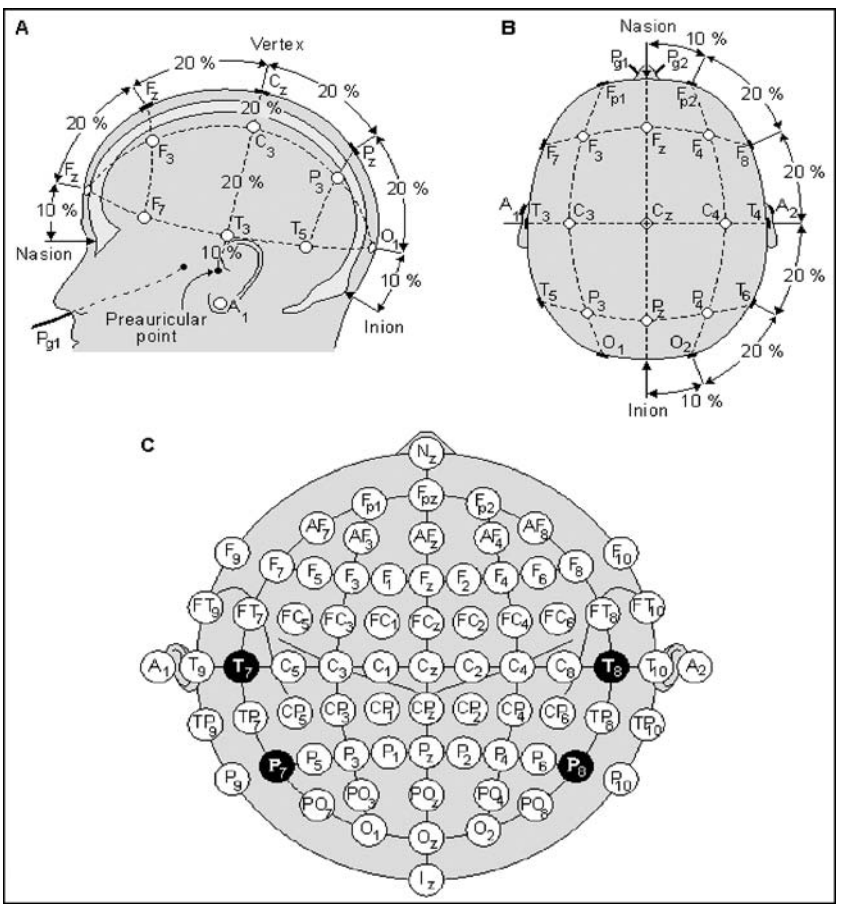


Fig. 74. The 10/20 System, which takes into account, the individual differences in circumference of the skull.

is placed below the level of spinal manipulation, thus monitoring the stimulus input. A 2-channel system can be effective using: Channel 1 at left popliteal fossa right popliteal fossa, and channel 2 at Cz′-Fpz (or C3′-C4′). Occasionally, a coronal scalp derivation (C'_3-C'_4) may have larger cortical responses than the sagittal derivation (Cz′-Fpz). The monitoring physician may wish to record both initially then use the best one for the remainder of the monitoring. The popliteal fossa (PF) is the posterior aspect of the knee between the tendons of the biceps femoris muscles on the lateral side and the tendons of the semimembranosus and semitendinosus muscles on the medial side. Cz′ is 2 cm posterior to Cz.

In selected cases of monitoring sciatic nerve function during pelvic surgery, the peroneal is the primary nerve to be monitored. This is because its division in the sciatic nerve is more easily affected than the posterior tibial nerve division during the sciatic nerve compression that occurs during pelvic surgery. Unfortunately, it is difficult to monitor a caudal site to determine stimulation effectiveness. The lumbar response is best used as a rostral monitor instead of the cortical response because of the stability it offers.

When one stimulator is being used, upper limb *analysis time* should be 50–75 ms, and lower limb analysis time should be 100–150 ms. If two stimulators are available and one can be delayed, then both sides can be evaluated on one screen by alternating stimulation during averaging. This method has been called simultaneous asynchronous stimulation.

The *number of transient responses* required per average depends upon the clarity of the averaged response and the comfort of the monitoring physician when evaluating the waveforms. As soon as the averaged response is clear (50–500 stimuli) then another can be started. Minimizing artifacts will decrease the time taken per average.

A *ground electrode* (plate, disk, cup, band, or subdermal needle) should be placed between the most distal stimulus site and the first recording site, to minimize line frequency, artifact and some stimulus artifact. Recording leads should be grouped together as tightly as possible and electrode-skin

impedances should be similar to minimize line frequency.

Artifact detection is an important aspect in minimizing interference. If for instance, the operating table is electrical, unplugging it may decrease excessive line frequency. Electrically operated equipment near the recording electrodes, such as infusion pumps and fluid warmers, may be located elsewhere if they are causing line frequency artifact. Administering a neuromuscular blocking agent to the patient, if this is compatible with surgery and anesthesiology can eliminate EMG artifact. For *infection control,* all electrodes should be properly cleaned, and sterilized prior to use on each patient. Electrodes that are intended for the sterile field should preferably be gas autoclaved, double wrapped if multiple items are packaged, and tagged with an expiration date.

For *electrical safety*, and if monopolar electrocautery is used during surgery, one must ensure that the neuromonitoring leads are distant from the cautery return lead. This will help minimize the chance of stray capacitances from the radio-frequency electrocautery unit, which could cause current flow in neuromonitoring leads. One has to make sure the evoked potential equipment used is electrically isolated from the patient contact parts, and that it has an isolation transformer. Also, one has to make sure that leakage current testing is performed routinely on all pieces of equipment.

Alarm criteria for standard spinal cord monitoring using SSEPs have often been suggested as a 50% decrease in cortical baseline amplitude, or 10% increase in cortical baseline latency when using the post-anaesthesia/pre-incision baseline as a comparison. The accepted criteria, however, should be agreed upon within the monitoring team in each institution. Other events that may result from neural compromise are unilateral changes and especially sudden changes that correlate to surgical maneuver or decrease in perfusion. The monitoring physician should be aware of the effect of all medications and anesthetic agents and communicate effectively with the surgeon, especially when a change in responses occurs, to determine the cause of the change.

For *trouble shouting* with small amplitude of the baseline at cortical response, one should check the anesthetic level. If it is high, one should evaluate lowering the anesthesia level. Alternating, the low-frequency filter is lowered, or the stimulation rate is lowered. In addition, the stimulus intensity can be increased (use the peripheral response amplitude to titer) and steps should be undertaken to decrease the electrical noise.

With an underlying neural pathology when monitoring spinal cord function, one should stimulate both sides together (two stimulators are needed). In case of high background noise and if EMG is the source, one should use a neuromuscular blocking agent. In addition, powered devices and power cords should be moved away from the recording leads. Also, recording leads, especially pairs, are wound together, the operating room table should be unplugged and one has to make sure, that impedances of recording electrodes match.

In case of high stimulus artifact the impedances of the recording electrode pair, especially if artifact is only affecting a few channels or one channel, should match, reapplying the ground electrode. Also, reapply stimulating electrodes and make sure they are connected properly. Replace the stimulating electrode if is suspected that one is broken. Move the recording electrode pairs closer together if possible. If there is a good motor twitch but no evoked responses, this could relate to an underlying pathology and thus is a limitation when monitoring, and one should check for a possible constriction of the nerve in the proximal limb (poor positioning, intermittent blood pressure cuff, tourniquet).

AUDITORY EVENT-RELATED POTENTIALS (AEPs)

Event-related potentials (ERPs) are brain responses time-locked to some "event". This event may be a sensory stimulus (such as a visual flash or an auditory sound), a mental event (such as recognition of a specified target stimulus), or the omission of a stimulus (such as an increased time gap between stimuli). When a stimulus, either a click or a tone burst, is presented to the ear, the nervous system produces a series of responses extending from approximately 1.5 ms to over 500 ms after the stimulus. This sequence of responses can be divided into three general categories on the basis of their latencies and anatomical origins.

Auditory-evoked potentials (AEPs) present a non-invasive evaluation of functional state of auditory nerve and brainstem auditory sensory pathways. While the audiogram evaluates the psychophysical perception being a subjective technique, the reflex tympanogram evaluates middle ear function, and the electronystagmogram (ENG) indirectly evaluates the vestibular division nerve VIII, brain stem evoked potentials (BSEP) present a useful tool for audiologic differentiation of conductive and sensorineural loss. The BSEP is also used for neurologic evaluation of the auditory division of nerve VIII and the auditory pathways through the brainstem.

When measuring AEPs the response which one wants to measure has a short latency (>50 msec), and a small amplitude (>1 μV). It therefore needs a fast stimulus, which will synchronously depolarize a large population of auditory neurons. The stimulus (event) is a square-wave click stimulus with a duration of 100–200 msec and an intensity of 70 dB, typical decibel intensity for the AEP stimulus,

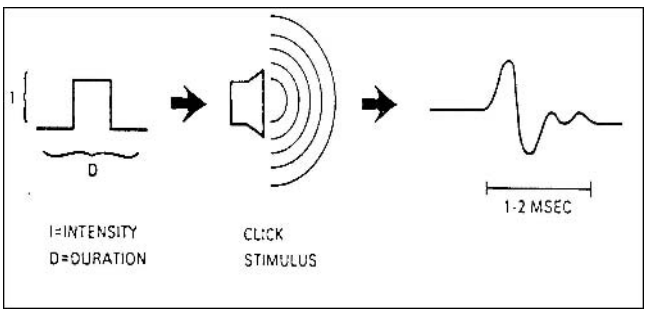


Fig. 75. Principle of auditory-evoked potentials using a click stimulus to activate the auditory sensory pathways.

using a polarity of positive electrical rarefaction pulse (Figure 75). To avoid bone conduction, the opposite ear is masked using 40–70 dB less than stimulus. For the earphones TDH-39 audiometric quality standard is advocated Noise-excluding case optional unless the room is noisy (>30 dB background). Different stimulating speakers will give different responses; therefore always use the soma kind of earphones. Check at least monthly for wear and deterioration of diaphragm within the earphones, replacement with a 300 Ω and not a 8 Ω speaker.

Possible artifacts, which may interfere with proper recording in AEPs

1. Pulse emitted by an electromagnet in the speaker using a click sound.
2. The duration of the click sound (the event) normally is less than 1 msec. However, it may in certain instances overlap with wave I in the acoustic, event-related potential.

What to do to eliminate artifacts:

1. Use an alternating click, which broadens the duration and shortens the amplitude of wave II.
2. Change the position of the speaker
3. Place the reference electrode on the inside of the earlobe or on the mastoid.
4. Reduce the electrode impedance, as lower impedance results in lesser electrical interference.
5. Shield the earphone with a grounded metal grill.

The generators in AEP is complex and many issues remain to be resolved (Figure 76).

Using an Az–Cz montage, the response of the AEP is characterized by a typical waveform with 7 different peaks, which grossly can be attributed to specific anatomical locations (Figures 77 and 78).

The origin of the different peaks are related to anatomical structures (Table 12):

Table 12. Summary of the different generators, which result in the formation of peaks in AEPs

Peak	Generator of origin
I	Action potential at cochlea
II	Auditory nerve
III	Olivary complex – cochlear nucleus (?)*
IV	Brainstem (?)
V	Lateral lemniscus
VI	Medial geniculate (?)
VII	Auditory radiations (?)

*(?) Indicates that discussion on the origins is still in progress and that no final conclusion has yet been reached among experts in this field.

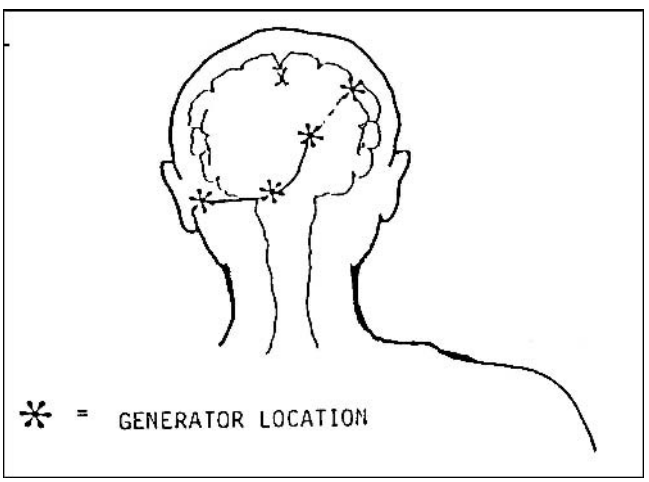


Fig. 76. Purported generator locations in AEP recording.

Due to the alleged generator location in AEP monitoring, a possible pathology can be identified:

I–III → Impedance of peripheral conduction, such as an acoustic neuroma.
III–V → Pathology affecting central conduction.
V absolute → Audiologic inquiry necessary in order to determine whether there is a sensorineural or conductive loss present.
P35 → This component indicates cortical arrival. It is the major peak of the Middle Latency Response.

The montage in AEP monitoring is summarized in the following table using specified instrument setting:

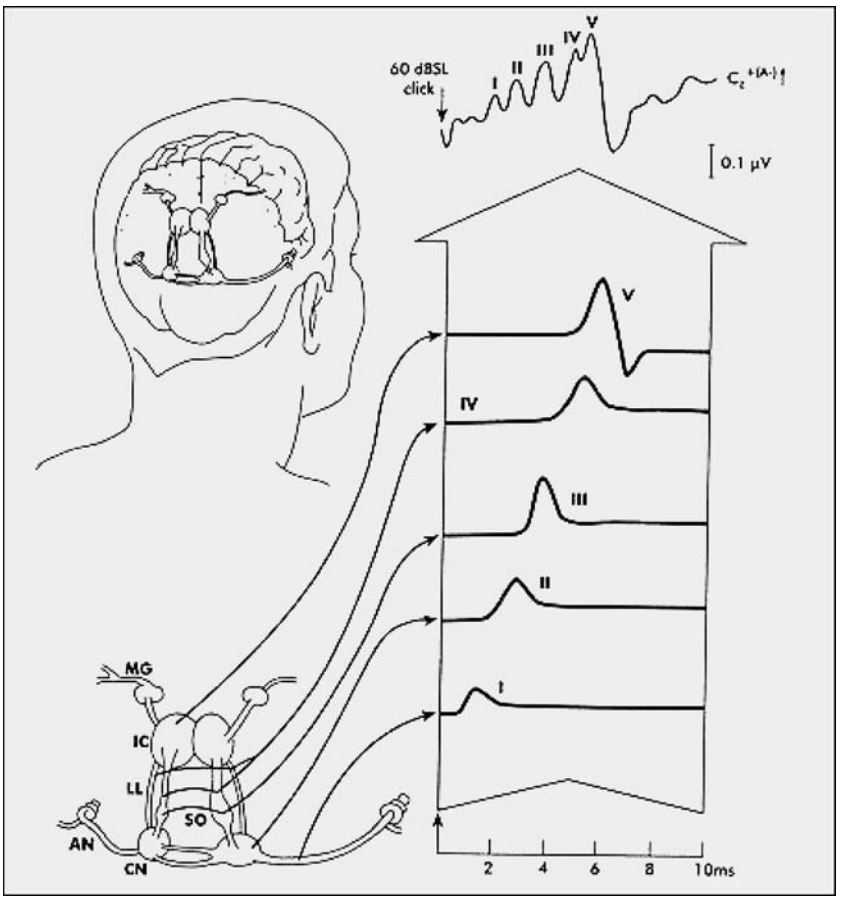


Fig. 77. Typical waveform in acoustic evoked potential recording with its main five peaks.

Montage	Standard	Optional 1	Optional IV–V
Active	A1	A2	Ac
Reference	Cz	A2	Cz
Ground	Fpz	Fpz	Fpz
Setting of the equipment			
Gain	10μV	Sweep	1 msec/div
Scale factor	20	Repitition rate	11.1/sec
High-cut	3000 Hz	Pulse duration	100 μsec
Low-cut	100 Hz	Artifact rejection	on
Averaging	1000	Stimulus	Click
Rarefication	70 dB		

Using the standard montage and the instrument settings as outlined above results are replicated twice for each ear and compared for consistency. If the waveform unclear:

(a) Probably no response? Check the following: Does the stimulus reach the ear? Is the stimulus being transduced at cochlea (run an audiogram)? Increase the click intensity of the stimulus, switch the polarity of the stimulus, or use new electrodes or use a different montage.
(b) To much noise in the event related acoustic recording, then do the following: Increase the number of averages. Check electrodes and environment for other electrical sources, use alternating click (shock artifact), increase patient relaxation, and administer a sedative if necessary.
(c) To enhance Peak I by minimizing artifacts, use a lateral montage, change the polarity, increase the intensity, use a canal electrode, and finally slow the repetition rate.
(d) To separate Peak IV–V by changing polarity, use a contralateral montage, and decrease intensity.

Evaluating the morphology of the measured waveform (see also Table 13):

Peak VI most prominent after 5.5 msec. If not decrease the intensity of the click sound with the last peak remaining. If Peak I shows a latency >1.4 msec, use the A1–A2 montage, which may resolve the problem. Peak III should have a equal distant between Peak I and V.

Table 13. Normative data of the acoustic evoked potentials (ABS = absolute values; IPL = interpeak latencies; L-R = left to right difference)

		Mean	S.D.
ABS	I	1.7	0.15
	III	3.9	0.20
	V	5.7	0.25
IPL	I–III	2.1	0.15
	III–V	1.9	0.18
	I–V	4.0	0.23
L-R	I–III	0.10	0.10
	III–V	0.10	0.11
	I–V	0.13	0.10

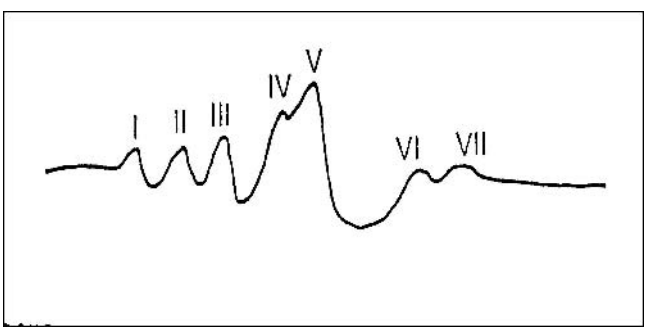


Fig. 78. The different peaks as they are displayed of the brainstem auditory (acoustic) evoked potentials (BAEP). AN = acoustic nerve, CN = cochlear nerve, SO = superior olivary, LL = lateral lemniscus, IC = inferior colliculus, MG = medial geniculate and the generators of these peaks of the different peaks: I – action potential at the cochlea; II – auditory nerve; III – olivary complex-cochlear nucleus; IV – brainstem; V – lateral lemniscus; VI – medial geniculate*; VII – auditory radiation*.*

Factors, which alter the response in event-related posterior tibial nerve stimulation

Non-pathologic stimulus factors that can alter the evoked response

1. As **click intensity** increases, latency is reduced. Latency increases by 0.03 msec per decibel of decrease in click intensity. Interpeak latencies do not change.
2. **Click frequency** affecting Brain Stem Evoked Potentials (BSEPs) are reflected best at 1000 Hz and upwards. Best results are obtained in the range 2000–4000 Hz. Watch for old headphones, as they are not able to deliver a sufficient high frequency rate.
3. A **repetition rate** of less than 10/sec gives clearest waves. A faster repetition rate slightly increases the latency. Also, a faster repetition rate can decrease amplitude and reconcilability, while the interpeak latency (IPL) increases slightly at high rates. In addition, the value of a "stress test" is unclear.
4. **Click polarity** is important as rarefaction shortens the latency of Peak I by 0.1 msec, whereas the latency of Peak V does not change.
5. In **filters setting** with a lower high-cut filter to 1500 has little effect, and increase in the slow component ranging 3 to 4 msec long (= 15–20 Hz) is of no clinical value. For better recording it sometimes it may be necessary to raise the low-cut filter to 300.
6. **Transducer characteristics** are of importance as hearing aids and intensifiers concentrate sound intensity, resonate differently than earphones. They are however, most useful in the OR and the ICU. Use of etymotic earphones result in a 1 msec absolute delay due to the tubing, and its frequency characteristic mimics TDH-39. Use of a bone vibrator bypasses conductive hearing loss, however, it is hard to control the intensity and there is the need of masking the noise in the opposite ear. Altogether, such use results in an increase in absolute latencies by 0.5 msec.

Non-pathologic stimulus factors that can alter the response

1. With increasing **age**, latency of components increases slightly in terms of absolute and interpeak latency as age increases. However, this shift is not enough to matter. When testing infants up to 6 months use a longer sweep. Typically after 6 months to 1 year responses are close to if not the same as adults.
2. **Gender**. Females have slightly shorter latencies than males. The responses diverge at the age of 8.
3. **Body temperature**. Absolute and interpeak latencies increase as body tempo drops. There is an increase by 0.17 msec/degree centigrade. If temperature falls below 27 degrees Celsius, all waveforms are lost.
4. **Peripheral hearing** loss results in an extension of absolute latency and a decrease of amplitude, while interpeak latencies remain unchanged.
5. **Sleep and/or the level of consciousness** have no effect on latency or amplitude height.
6. **Medication** in general has no effect. However, all anesthetics, especially if they induce hypnosis result in an increase of latency and a decrease in amplitude, which at higher concentration may be lost altogether. Ototoxic drugs (i.e. gentamycin) will degrade the BAEP. Alcohol has an indirect effect, as there is a drop in temperature.

A report on AEP should be separated into:

1. The audiologic report, where absolute latency of wave V, left to right difference in wave V latency is given. Detailed Evoked response audiometry requires measurement of latency-intensity curve or a 40-Hz test.
2. The neurologic report with interpeak latency values and left to right interpeak latency differences.

The brain-stem evoked potential (BSEP) protocol

Every evoked potential measurement should include a protocol in order to know later what stimulus parameters have been used, the settings of the instrument and type of electrode montage chosen

1. **Stimulus parameters**

   DURATION – 100 msec
   REPETITION RATE – 11.1/sec (to avoid 60-Hz multiple)
   INTENSITY – 75 dB nHL
   THRESHOLD – 0 dB nHL
   MASKING – 0 dB nHL

2. **Instrument parameters**

   GAIN – 10 to 20 μV/div
   HIGH-CUT FILTER – 3000 Hz
   LOW-CUT FILTER – 100 Hz
   SWEEP SPEED – 1 msec/div (10-msec epoch)
   SCALE FACTOR – 20
   AVERAGES – 1000 or 2000
   ARTIFACT REJECTION – On

3. **Electrode montage**

   ACTIVE - earlobe (ipsilateral) on the same side as the stimulus
   REFERENCE – Vertex (Cz)
   GROUND – earlobe on the opposite from the stimulus (contralateral) or Fpz

   Note: When the stimulus is switched from one ear to the other, ACTIVE and GROUND must also be reversed.

4. **Patient** – check each ear canal for possible obstruction or perforation. Apply electrodes and check impedances as they should be below 5 kΩ. For the measurement the patient should be in a reclined position, in a dimly lit room, wearing the headphones. One has to make sure that the headphones are directly placed over the ear canal. Then present the acoustic stimuli and observe on-line the responses on the screen of the instrument. Watch for artifacts such as

   (a) Large amplitude random waves
   (b) A regular hum or spikes
   (c) A flat line

To eliminate the causes of noise check the electrode impedances (as they present the major source), tell the patient to relax, turn off all nearby electrical equipment, especially motors, TV monitors and fluorescent lights.

When collecting the evoked response monitor at least two replications on the display and evaluate for reproducibility by:

(a) Superimpose replicated waveforms
(b) Identify peaks I through VII
(c) Measure peak latencies (stimulus to peak) and
(d) Amplitude height (peak to peak) by using the cursors for identification
(e) Compare latencies and amplitude height with normative values
(f) Compute the central conduction time (peak I to peak V, I to II, and III to V)
(g) Compare the CCT with normative values
(h) Compute the amplitude ratio of waves V to I (the ratio should be >0.5 msec)
(i) Print out the waveforms.

Possible problems that may arise during the measurements

1. No responses? Then listen to the clicks, is the stimulus reaching the patient? Ask the patient if he/she can't hear the stimulus.
2. Peak I cant be identified. Make sure that the stimulus reaches the right ear.
3. The stimulus obscures peak I, if this happens use alternating clicks.
4. In case of other problems evaluate the response on the screen when changing either stimulus intensity, stimulus type, click polarity and duration, repetition rate, or sweep speed (2 msec/div) respectively.

AEPs reflect the sequential activation of the VII nerve (N. acusticus). Thus, all elements of the auditory brainstem pathway can be monitored (BAER). In this modality, a square wave pulse is emitted by an electromagnet through earphones (dick stimulus) of 100–200 μsec duration. The response waveforms as they are recorded by the electrode montage (active = earlobe on the same side as the stimulus = ipsilateral; reference electrode on the vertex = Cz; grounding on the frontal head = FpZ) results in seven characteristical peaks which more or less can be attributed to specific sites of origin along the primary auditory pathway (Figure 81).

Auditory evoked potentials (AEPs) are a subclass of ERPs (Event Related Potentials). For AEPs the "event" is a sound. AEPs are very small electrical voltage potentials originating from the brain recorded from the scalp in response to an auditory stimulus (such as different tones, speech sounds, etc.). The AEPs that are recorded from the top of the head originate from structures within the brain (e.g., the auditory cortex, the auditory brainstem structures, the auditory VIIIth cranial nerve). They are very low in voltage: from 2–10 microvolts for cortical AEPs to much less than 1 microvolt from the deeper brainstem structures. Their low voltage combined with relatively high background electrical noise requires the use of highly sensitive amplifiers and computer averaging equipment.

The earliest group of responses, occupying the first 10 ms post stimulus, is known as the short-latency auditory evoked responses, which arise from the brainstem structures in the rostral medulla, pons and caudal midbrain. The components of the short-latency or brainstem auditory evoked responses (BAER) can be used to measure the functional integrity of brainstem structures, particularly those located in the pons. The BAER can also be used to estimate hearing thresholds in those individuals who are not appropriate for behavioral audiometric evaluations. These may include, but are not limited to, retarded and very young children. A component of the BAER, wave I of the action potential of the VIII nerve, may also be recorded in greater detail using special ear canal electrodes. This technique is known as electrocochleography and allows detailed study of both the action potential of the VIII nerve and the summating potential, which precedes it. Comparison of the relative amplitudes of these two components provides information on the functional integrity of the cochlea. A second group of responses from the 10–60 ms post-stimulus are known as the middle-latency auditory responses (MLAER). These responses are thought to arise from the medial geniculate nucleus of the thalamus and from the primary auditory cortex. While these responses have been of limited use for neurological application, they have been found to be useful for audiological purposes. In addition, recent evidence suggests the middle-latency responses to be of value in diagnosing learning disabilities.

A possible derivative of the middle-latency auditory response, the 40-Hertz auditory event-related potential, has been shown to have audiologic and neurology applications. This response is sensitive to lesions involving medial midbrain structures and is also useful for determining hearing thresholds, particularly to low frequency (below 100 Hz) tones. The third groups of responses, extending to 500 ms and beyond, are the long latency auditory responses. While the precise anatomical origins of these long latency responses are unclear, they are thought to represent the activity in cortical association areas. Long-latency auditory responses are used primarily for audiological and psychological purposes.

The AEP can be differentiated into different peaks, which originate from different nervous structures (Figure 79):

1. The **Brainstem Auditory Evoked Potential** ("BAEP"; 1.5–15 ms post stimulus) Figure 83, which originates in the VIIIth cranial nerve (waves I and II) and brainstem auditory structures (wave V: region of lateral lemniscal and inferior colliculus).
2. The **Middle Latency Evoked Response** ("MLAER", 25–50 ms poststimulus) includes waves Na (negative wave following ABR wave V, originates in upper brainstem and/or auditory cortex) and Pa (positive wave at about 30 ms, originates in the auditory cortex bilaterally).
3. The "**Long-Latency Auditory Evoked Potentials**" of cortical auditory potential, which include the P1-N1-P2 sequence (LLAEP 50–200 ms poststimulus; originating in auditory cortex). N_1 is the large negative wave that occurs about 80–100 ms after the stimulus. It originates primarily in the auditory cortex bilaterally. In the figure to the left, it is the large negative wave seen both in the response to the "standard" (black line) and the "deviant" (or oddball; red line) stimuli.
4. The "**Late**" cortical auditory potentials, especially the **Mismatch Negativity** ("MMN"; beginning around the time of N_1 *and* later). The MMN is a response reflecting detection by the brain of a *change* in the stimulus. In the figure to the left, the MMN is the increased negativity seen in the response to the deviant or change stimuli (red line), at about the time of N_1 and a little later. Other "late" potentials not present in these waves include "N_{2b}" and "P_3", which are cortical potentials, not being specifically derived from auditory structures.

The auditory steady-state responses (ASSR)

This is a very different type of auditory evoked potential are which are responses to stimuli presented at rates such that the brain response to one stimulus is overlapped with responses to other stimuli. Responses to slower modulation rates (<20 Hz) appear to originate largely in *cortical* structures; responses to faster rates (70 Hz and higher) appear to reflect *brainstem* processes. ASSRs to rates >70 Hz show great promise for rapid assessment of hearing in the infant. The multiple-auditory-steady-state-evoked-response (MASTER) technique provides a rapid and objective assessment of hearing. The technique is based on the statistical evaluation of the electrophysiological responses evoked by multiple auditory tones presented simultaneously. These

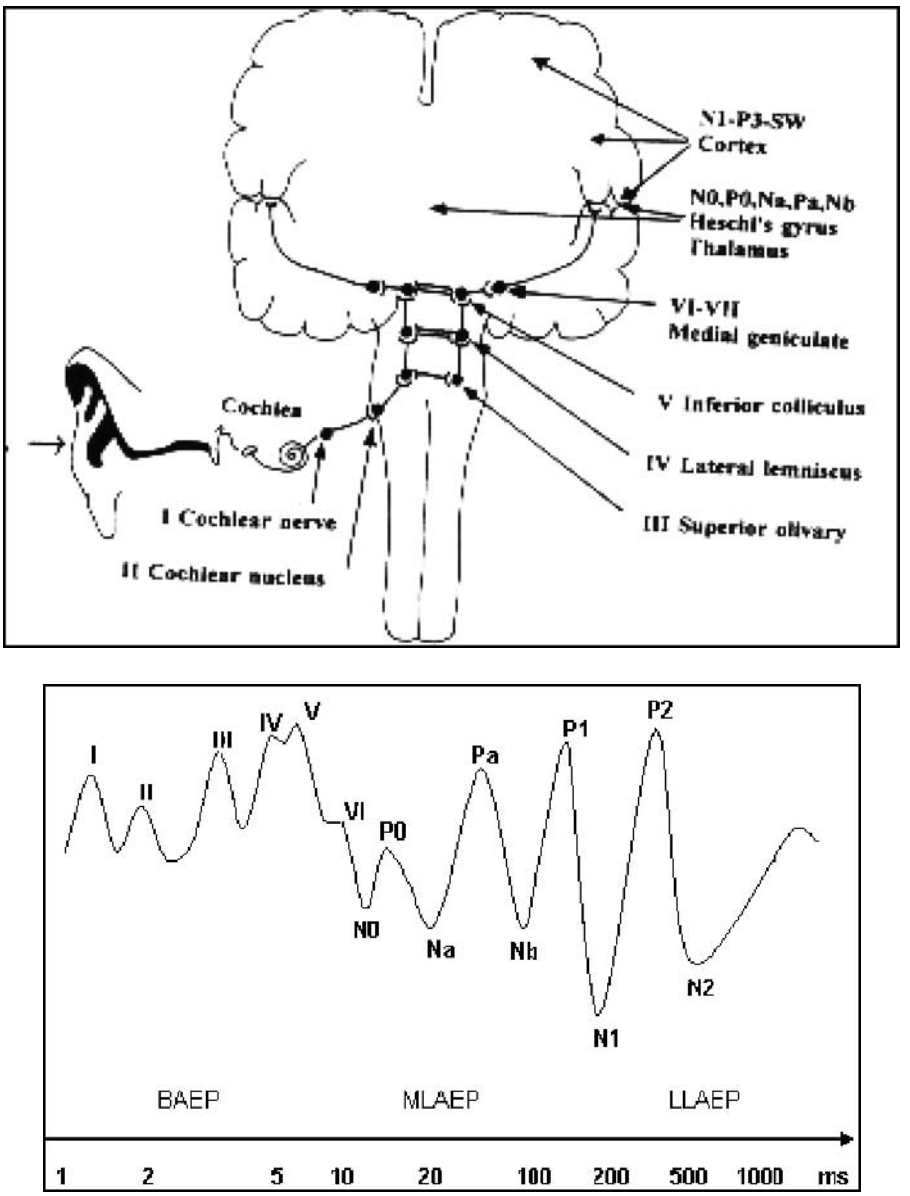


Fig. 79. The different subgroups in auditory evoked potential, their generators and the terminology of the different peaks: I – action potential at the cochlea; II – auditory nerve; III – olivary complex-cochlear nucleus; IV - brainstem; V – lateral lemniscus; VI – medial geniculate*; VII – auditory radiation*. *Indicates that the discussion of the origin is still in progress and no final conclusion has yet been reached.*

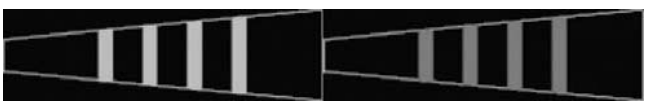
auditory steady state responses can be recorded from the human scalp intermixed with the other activity in the electroencephalogram (EEG). A combination of averaging and frequency-analysis can distinguish the responses from the background EEG. MASTER typically presents 8 continuous tones (4 to each ear) and each tone is sinusoidally modulated at a unique frequency. The detection of the interwoven responses becomes possible after the electrophysiological data are transformed into the frequency domain. MASTER evaluates the responsiveness of the auditory system to several tonal frequencies in the same time it would take to record one response if each stimulus were presented separately. The Multiple Auditory steady-state response (MASTER) technique enables multiple tones to be tested at the same time. The figure shows four stimuli that will be presented to the left ear and four stimuli presented to the right ear. The carrier frequencies are 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz and the modulation

frequencies for the left ear (77, 85, 93, 101) must be different than those for the right (79, 87, 95, 103).

	Modulation (Hz)	
Carrier (Hz)	Left	Right
500	77	79
1000	85	87
2000	93	95
4000	1001	105

The four separate stimuli are combined in the time domain and are presented to the subject as complex tonal stimuli.

At the cochlea the following different response are initiated.



This is because the cochlea is tonotopically organized and the 4 tones are each sensed by the respective tonal area on the basilar membrane.

The hair cells in each tonal area fire with the maximum of the AM envelope for each tonal frequency, and therefore the evoked steady-state responses are produced at the frequency of modulation of each carrier frequency. The signals are compared to background EEG activity (grey in figure) using the *F*-ratio statistic, and if the signal to noise ratio is large enough, a response is considered significant (i.e., the subject heard the tone).

In addition to being a diagnostic tool, AEPs can also be used for the evaluation of drug effects on the auditory afferences. An example in the following figure demonstrates their utility in alcohol intoxication and its reversal with high doses of the potent opioid antagonist naloxone.

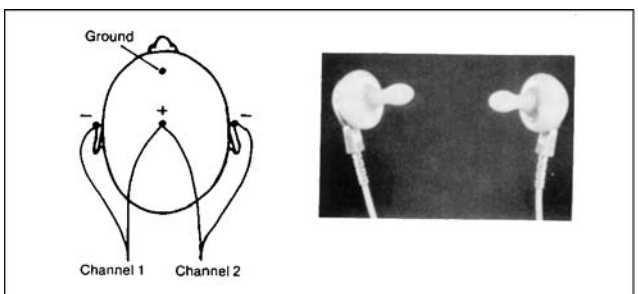
Practical considerations when using AEPs in the OR

The following procedure is advocated in order to get a good signal from the auditory pathway. Using the standard montage (right ear: A_2-Cz, ground FpZ; left ear: A_1-Cz, ground FpZ) with an instrument setting as listed in the following figure (Figure 80). Results should be replicable for each ear and compared among each other for consistency. If no response to the click is seen on the display, the following points should be verified:

1. Check whether the stimulus reaches the ear as the earphones have to be over the external ear canal.
2. Check for obstruction or perforation of the ear (can the patient hear the stimulus?).
3. Increase click intensity of the stimulus.
4. Make sure whether the stimulus is transmitted at the cochlea (run an audiogram).
5. Try while switching the polarity of the electrode.

If the noise on the display wave is too intense:

1. Increase the number of averages.
2. Check electrode impedance (set it below 3 kΩ).
3. Twist the electrode cables together as they may act like antennas picking up electrical noise from the environment.



Recording parameters	Stimulation parameters
Channel 1 : Cz – A1	Era-insert transducer
Channel 2: Cz – A2	Clicks with alternating polarity
Ground: FpZ	60 dB SL (personal threshold)
Filters: 30 – 3000 Hz	200 μsec duration
Sensitivity: ±25μVolt	Contralateral masking
Full scale	Noise: 35 dB Hl
Sweep time : 10 – 24 msec	(average threshold)
Sampling rate : 50 KHz	
Repetition per average: 2000	

Fig. 80. Brainstem auditory evoked potentials with placement of electrodes and stimulation parameters.

4. Eliminate surrounding electrical noise by turning off nearby electrical equipment, especially all motors, TV monitors, and fluorescent lights.
5. Administer a sedative to relax the patient.
6. Use alternating clicks.

During the measurement the various peaks should read as follows:

1. Wave V is the most prominent and appears around 5.5 ms post stimulus.
2. Wave I should have a latency of less than 1.4 ms. It is of no use in contralateral montage.
3. Wave III should have an equilatency between the foregoing wave I and wave V.

The following factors may influence the different waves in BAEP:

1. Latency increase by about 0.03 ms per dB of decrease.
2. Best results are obtained with a click frequency from 2000–4000 Hz as BAEP reflect 1000 Hz and up.
3. A repetition rate of 10 per sec gives the clearest waves. A faster repetition rate can decrease amplitude and reconcilability. Also, interpeak-Latency (IPL) increases slightly at higher rates.
4. Hearing aid stimulators are more useful in the OR and ICU setting than headphones. They, however:

    a. Intensify sound,
    b. Resonate differently than headphones, and
    c. Show an absolute delay of around 1 ms due to the tubing.

5. The bone vibration, which comes with the dick sound, bypasses any conductive loss.

Because of this bony vibration, a masking noise is needed in the opposite ear while stimulation on one ear will be picked up. Factors, which will affect the response, include:

(a) Body temperature: Absolute and interpeak latencies increase as the body temperature drops (0.17 ms/°C). If the temperature falls below 27 °C, all waveforms are lost.
(b) A peripheral hearing loss will extend the absolute latencies and decrease amplitudes.
(c) Drugs in general have no effect except all ototoxic drugs (i.e. gentamycine) which degrade the AEP.

An analysis report of the AEP will be devided into:

(a) Audiological, with absolute and left to right latencies of wave I, while a detailed evoked response audiometry requires measurements of latency changes or the 40 Hz test (see above).
(b) Neurological, with interpeak latencies (stimulus to peak), left to right interpeak latencies differences, and a computation of the conduction times (CCT) of wave I to V, I to II (peripheral conduction time), and II to V (central conduction), which will be compared with normative values.
(c) The absolute value of wave V. An additional audiological inquiry determines whether a sensorineural or a conductive loss is present. The interpeak latency of wave V to I should read less than 0.5 ms.
(d) The P_{35} component indicates cortical arrival. It is the major peak of the middle latency response.

Summary of guidelines in acoustic evoked potential monitoring

Whenever possible the performance of preoperative baseline studies in the modality to be monitored are recommended. The baseline study can be performed in the clinical lab prior to the surgical admission or, less desirable, in the patient holding area before entering the surgical suite. The benefits of the baseline study include: identifying preoperative dysfunction that might predict operative risk, identifying additional neurological disease that might preclude normal (or useful) monitoring activity, and serving as the standard to measure subsequent postoperative changes against.

A stable post-anaesthesia/pre-incision baseline monitoring trace should be secured prior to the surgeon's initiating the operative procedure. This intraoperative baseline should be obtained after the patient's desired anesthetic state is achieved. The baseline should then be stored for review and comparison as the case progresses. In addition, continuous monitoring of the EEG and evoked potential should begin before the initiation of the surgical procedure and proceed continuously throughout anesthesia. Some recording parameters in place for EEG monitoring may need adjustment to conform to the developing patterns; however, parameters and stimulation techniques should not change during evoked potential monitoring. Throughout monitoring, close observation of the waveforms will reveal the presence of difficulties relating to the OR environment, instrumentation, electrodes, and patient artifacts. The rapid assessment and, if possible, elimination of artifacts and malfunctions are essential for the validity of the ongoing monitor. If a change occurs in the waveforms being monitored, and the cause is believed to be of technical origin, the surgeon must be notified if the time required

to identify the source exceeds the warning time established between the surgeon and monitoring physician.

For documentation purposes, the monitoring physician maintains a written record of the following (and their relationship to changes in the monitored waveforms): changes in anesthetic levels, the surgical procedure and any manipulations, and changes in the patient's physiological state such as blood pressure, temperature, etc. The final summary report is the responsibility of a qualified neurophysiologist. Use of alarm criteria is the responsibility of the monitoring team to establish communication guidelines for relating changes that may occur in the monitored waveforms. The criteria should outline what is considered a significant change in amplitude and latency for evoked potential monitoring, and in waveform patterns and contrasting hemispheric changes for EEG monitoring.

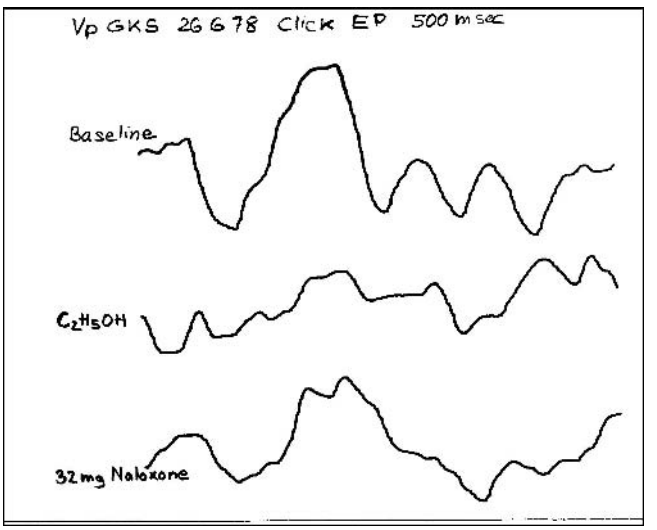


Fig. 81. Example of a subject intoxicated with alcohol (2.4‰) where the drug induced a depression of all peaks. This effect was reversed by naloxone suggesting either a non-specific activation of brain stem neuronal activity or a displacement of alcohol metabolites (i.e. tetraisoquinolines) from the opioid receptor. Adapted from [35].

CLINICAL APPLICATIONS OF BRAINSTEM AUDITORY EVOKED POTENTIALS

Brainstem auditory evoked potentials (BAEP) are utilized during neurosurgical procedures that involve the pons and the lower midbrain. The intent is to protect these areas from damage that could lead to serious, permanent, neurologic deficits. The recording of direct nerve action potentials from the exposed 8th cranial nerve and cochlear structures in cases such as microvascular decompressions and acoustic nerve tumor resections also can help preserve hearing.

Brainstem pathology is characterized by abnormal latencies and/or amplitude suppression of peaks generated rostral to the site of dysfunction. Thus, BAERs are useful in the following situations:

(a) Acoustic pathway lesions caused by tumor or retraction such as during operation,
(b) Brainstem evaluation such as for brain death,
(c) Neonatal auditory sensory evaluation,
(d) Hearing evaluations,
(e) Demyelinating disease,
(f) Comatose patients (Figure 81), and
(g) Operation at the cerebello-pontine angle.

As brainstem auditory evoked potentials are subcortical in origin and are little affected by anesthetics, they can virtually be used with any anesthetic technique for monitoring. Absence of BAER in a comatose patient may be due either to neurological dysfunction or to conductive or sensorineural hearing loss. Additional recording of the electrocochleogram can only make a distinction between the two. If no electrocochleogram can be recorded, one must assume that the absent BAER results from peripheral hearing loss rather than from intracranial pathology. A correlation between intraoperative changes in BAEP or BAER (brain stern auditory evoked response) and postoperative brain damage fit with the current knowledge about the various generators of the BAEP waveform. Peak I which is generated in the extracranial portion of the auditory nerve and peak II which is generated in the intracranial portion of the auditory nerve and/or the cochlear nucleus could be preserved even in the presence of an injury rostral to the position in the brainstem (Figure 82).

Thus, one cannot exclude extensive cortical damage even in the absence of alterations in BAEP, as they do not reflect cortical function. BAEP are also very insensitive to hypoxia and are normal at oxygen saturations which otherwise will alter the cortical evoked potential [36]. In assessing the value of the BAEP monitoring during operations on the posterior cranial circulation, reports suggest this modality of EP recording to be a sufficiently sensitive device to evaluate stigmata of ponto-medullary dysfunction [37].

Basics for recording when being in the OR

In BAEP monitoring type standard EEG cup electrodes, adhered to the scalp with collodion and filled with a conductive gel, are recommended in most cases. During some surgical procedures, however, the scalp site for electrode placement is within the area of the sterile field. In these cases, subdermal (needle) electrodes may be preferred since

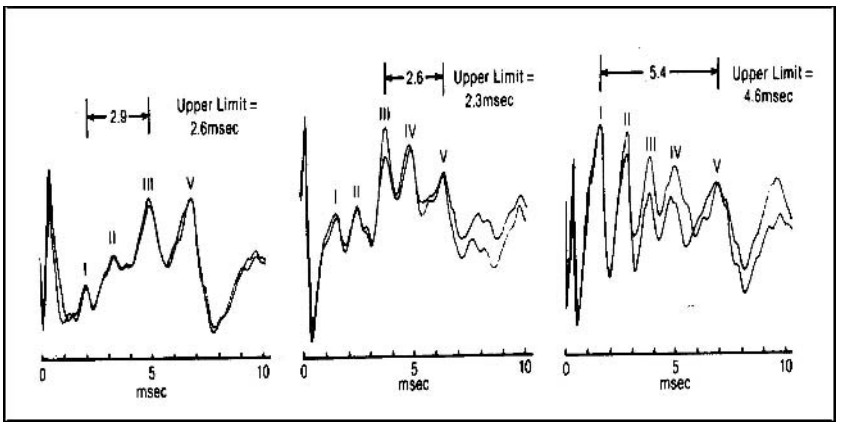


Fig. 82. The use of BAER peak latencies for the diagnosis of sensory dysfunction affecting the VIII nerve. Left: acoustic neuroma; middle: midbrain tumor; right: demyelinating disease (adapted from Nicolet Diagnostic Series).

they are sterile and insert quickly. In the cases of direct 8th nerve recording, the surgeon directly applies a wick or wire electrode to the exposed 8th nerve or through the tympanic membrane cochlear promitory.

Electrode Placement is over the left and right earlobes (A_1 and A_2 position according the International 10/20 System of Electrode Placement); or over the left and right mastoid processes. At the vertex location on the scalp, designated as Cz in the 10/20 System, the Cz electrode can be moved anteriorly to avoid the surgical field. The ground electrode is placed at Fz or Fpz of the International 10/20 System using a low filter setting of 10 Hz to 30 Hz (−3 dB) with a filter roll off not exceeding 12 dB/octave. High filter setting is 2.5 to 3 kHz (−3 dB) with a filter roll off not exceeding 24 dB/octave. Whenever possible, filters should be kept constant throughout the monitoring to eliminate filter related phase shifts, which alter latencies and can lead to erroneous interpretations. When recording in the operating room, it may become necessary to change filter settings in response to an electrically hostile environment and changes in the patient's physiologic state. Changes made to any instrument setting must be noted on the tracing and on the work sheet. Analysis Time is 10 to 15 milliseconds from stimulus onset, using 1000–4000 individual trials.

For stimulators a sponge or foam ear inserts are suggested for use in the operating room because of their small size and placement away from the surgical field. The inserts should be placed before surgical draping, then covered with waterproof tape or bone wax to secure them and protect them from fluids. The inserts are connected to the transducer by a plastic tube (approximately ten centimeters in length), which should be checked for kinks or compression that could obstruct delivery of the stimulus to the molded insert.

Otoscopic visualization of the canal and tympanic membrane must be carried out (by a qualified practitioner) to ensure a clear stimulus pathway. Excessive waxy secretions must be cleared from the external auditory canal before inserts or headphones are applied. The preferred type of stimulus is that of broadband clicks and should be generated by a 100 ms rectangular pulse (single, monophasic, square wave). Clicks of alternating positive and negative polarity are recommended to diminish stimulus. Stimulus intensity suggested is 100 decibels with peak equivalent sound pressure level or, alternately 60 to 70 dB HL with HL referring to hearing level, defined as the mean hearing threshold established through a group of normal subjects using the same monitoring equipment.

Stimulus rate is variable at 5 to 50 stimuli per second. Rapid assessment in the operation room is essential and can be performed at high rates when Waves I and V are being monitored. Clicks should be delivered to only one ear at a time and a masking noise delivered to the non-stimulated ear.

A minimum of two-channel montage is recommended for recording, with three channels being desirable. The recommended two-channel montage is channel 1 vertex to ipsilateral ear lobe or mastoid (Cz-A1 or Cz-Mastoid) and channel 2 montage is vertex to contralateral ear lobe or mastoid (Cz-ear lobe or Cz-mastoid). For a three-channel montage channel 1 is vertex to ipsilateral ear lobe or mastoid, channel 2 is vertex to contralateral ear lobe or mastoid, and channel 3 is left ear lobe to right ear lobe (A_1-A_2).

A preoperative baseline BAEP should be recorded from the patient prior to the day of surgery to verify the patient has a reproducible brainstem auditory evoked response. The patient's postanesthesia/pre-incision BAEP recording will act as the baseline tracing to which all intraoperative

recordings will be compared. Latencies with ear inserts will need additional time for the stimulus to reach the eardrum via the plastic tube.

Acoustic evoked potentials in monitoring depth of anesthesia; the AAI™-monitor

The AAI™ Monitor (Donmoter/Denmark) brought a new dimension to the monitoring of patient awareness under anaesthesia. At introduction in year 2000 it was the first commercially available device of its kind to use AEP technology, it is fast acting and its active technology brings new accuracy to the measurement of consciousness. By adding EEG extraction and processing to the known AEP principles the AEP Monitor/2 completes and enhances consciousness monitoring, designed to meet the needs of the modern operating environments, the AAI-monitor includes the following features:

- A specific neurophysiologic indicator,
- Operates independently of the anesthetic being used,
- Offers a maximum sensitivity and specificity,
- Burst Suppression and EMG indicators,
- Automatic check of auditory stimulation,
- Allows close to real-time detection of transitions from awake to asleep and recovery,
- Operates independent of baseline adjustment, and lastly
- Is highly cost-effective

In addition the device offers the following features

1. Event-related acoustic stimulation is done 9 times/second.
2. The EEG is measured by 3 low-cost disposable ECG electrodes.
3. The AEP, embedded in the EEG, is extracted using ARX modeling.
4. The AAI™ index within the range 100–0 is calculated automatically.
5. A signal-quality indicator gives information on the level of noise in the extracted EEG (Figure 83).

AEP algorithm actively evaluates the brain's reaction to acoustic stimuli. It's the natural choice for measuring patient consciousness under anesthetic because hearing is the last retained sense during anesthesia and the first to be regained prior to waking. Re-useable headphones/ear phones deliver the active stimulation; cost-effective disposable surface electrodes are used to measure the AEP. The result is instantaneous to accurately display the patient's level of consciousness.

Extracting the AEP from background EEG during anesthesia

Auditory Evoked Response is a response to an acoustic stimulus. The response, seen as waveforms is often divided in three sections (Figure 84):

- Brainstem response

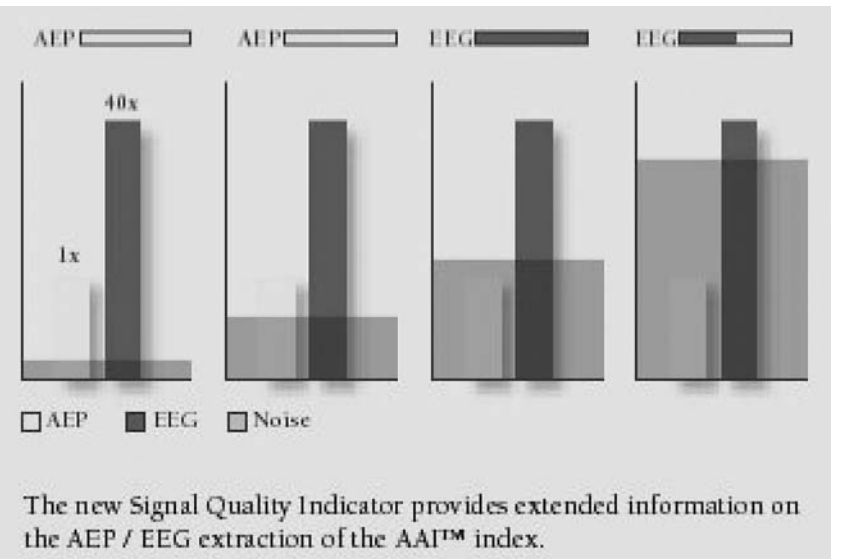


Fig. 83. Signal-quality indicator for additional information during evaluation of the hypnotic state using the AAI™ index.

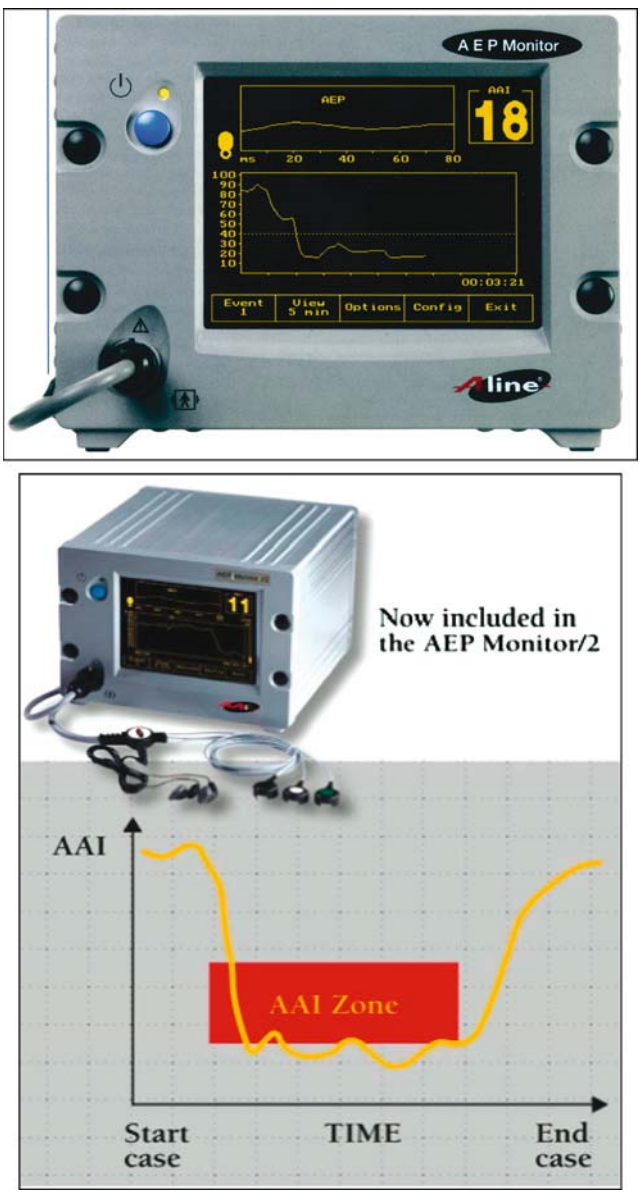


Fig. 84. The AAI™ Monitor (Danmeter/Denmark) with the AAI-zone for measurement of sedation level during anesthesia.

- Middle latency (early cortical) response
- Late cortical response

The Brainstem response waves occur within the first 10 ms after the click stimulus. These responses are relatively insensitive to general anesthetics. The middle latency waves occur 10 to 80 ms after the click stimulus – the AAI-monitor extracts these middle latency acoustic potential in the 20–80 ms window. Within this time frame any increase in general anesthetics in the clinical concentration range results in a graded decrease of the hypnotic state index. Late cortical changes occur 80 ms and over following click stimulus. These potentials disappear at sedative concentrations of general anesthetics.

AEP is a weak electrical signal wrapped in the EEG background activity. Extraction of the AEP requires advanced signal processing. Traditionally the MTA (Moving Time Average) method is used, which requires up to 1000 repetitions of the stimuli before the signal can be processed. This is a time-consuming process, which can result in a delay of approximately 2 min. The AEP Monitor on the other hand, uses a proprietary mathematical method called ARX modeling which can extract the AEP within just a few repetitions [38]. This reduces the delay, producing a processed signal as little as within few seconds.

To quantify the level of consciousness, the AEP is mapped into an index – the AAI index – within a range 100–0. The extracted AEP consists of several peaks of which the amplitude decreases, and at the same time the latencies of the peaks increase, with increasing concentrations of the anesthetic. These peaks are identified in the 20–80 ms range, corresponding with the Middle Latency AEP (ML-AEP).

The AAI preserves these two rules and the resultants value is based on the following premise:

- Validity for the largest number of subjects possible, independent of surgery and anesthetics
- Little overlap between index values measured while awake and asleep, which clearly differentiates between consciousness and unconsciousness

The EEG information is used *only* when the AEP is suppressed and therefore unable to provide further information. In such cases, the monitor takes advantage of the spontaneous EEG as the only available source of information. In an anesthetized patient, consciousness depends globally on all the factors acting on him/her: drugs, analgesia and different stimuli, etc. When calculating the AAI, the AEP information has priority in the algorithm, as this is the parameter that best describes the state of consciousness of a patient. When not using headphones, all this information is lost, leaving only the spontaneous EEG for analysis, which is mainly related to changes in hypnotic drug concentration.

The composite AAI™ index for measuring the level of consciousness

The AEP Monitor/2 measures the level of consciousness under anaesthesia based on the analysis of the electrical activity of the brain. The composite AAI™ Index combines the information derived from two different sources:

The AEP response elicited by acoustic stimuli, which has shown good correlation with transitions between consciousness and unconsciousness. This measurement is closely related to the level of consciousness of the patient. On the other hand, spontaneous EEG activity has shown good correlation with the effect site concentration of hypnotic drugs on the brain. Both EEG-derived measurements contain important mutual and independent information. In this sense, the AEP Monitor/2 is tooted to combine the better of two worlds.

Because of its different algorithm and by using the brainstem response, the AAI-index is said to show a better reflection than the bispectral index (BIS) when agents in anesthesia are used, which induce an activation in the beta-band of the EEG (i.e. benzodiazepines, propofol) but in reality result in a loss of consciousness in the patient (Figure 85).

The development of this new technology has significant benefits not only for the anesthesiologist, but also for the surgeon, the patient and the hospital. This is because the AAI Monitor allows the anesthesiologist to respond quickly, helping him to ensure the patient's safety and allowing the surgeon to continue the procedure. Because of the fast response on the level of hypnosis, the AAI Monitor is tooted to keep the anesthesiologist informed faster and similar to the other "anesthetic depth" monitors (BIS, Narcotrend, PSA 4000) it is said to improve patient recovery time, reducing anesthetic drug consumption, resulting in an earlier discharge from the PACU with less time spent in hospital, which in return, keeps hospital costs down [39–42].

THE VISUAL EVOKED POTENTIAL (VEP)

Visual evoked potentials (VEPs) present a noninvasive evaluation of functional state of the optic pathways and the visual cortex.

In contrast visual acuity and sensitivity tests-concentrate on foveal vision, perimetry concentrates on limits of peripheral visual pathway, and the electroretinogram (ERG) determines retinal function, the VEP evaluates the functional state of foveal paths between retina and cortex. Therefore, it is useful tool in search for organic evidence of deficit.

The stimulus in VEP is either:

(a) A luminance change (flash VEP), which results in large variance in normal response times; thereby providing a poor differentiation of abnormal responses. The clinical utility of flash VEP therefore is limited to answer the question if pathways to cortex are intact, compare left-to-right side, and it is useful in infants, patients with low vision, and the uncooperative patients.
(b) Pattern-reversal checkerboard stimuli, which project a constant luminance in pattern presentation with greater contrast, where white is bright as possible, and black is dark as possible, limiting contrast variation as much as possible.

The check size is 15 min to 1° of visual angle size. 30 min is considered to be the appropriate check size.

In regard to field size, the pattern should be as large as possible using 8°, which gives 80% of response amplitude (Figure 86).

In addition, reversal speed should be as abrupt as possible, which allows for such factors as use of a TV screen with 20–30 msec to change. In contrast, the light emitting diode (LED) stimulator, which is used in the OR, reverses pattern much more rapidly. The color in the checkerboard TV is black and white, while the LED is red. A fixation point is both used in TV and LED stimulators to hold eyes in center of field during pattern reversal presentation. The ambient lighting should be low enough so as not to wash out the pattern. Although cortical magnification dictates the VEP response, the majority of visual cortex reflects foveal perception. The N_{70} peak in the response waveform (Figure 87) is often difficult to identify, the N_{136} peak is inconsistent and the P_{100} peak is prominent and consistent in all subjects.

All waveforms are generated from the primary visual cortex, before higher association areas. No sub-cortical potentials have been found yet.

The protocol when deriving VEPs

1. **Instrument settings**

GAIN – 20 μV/div
HIGH-CUT FILTER – 100 Hz
LOW-CUT FILTER - 1 Hz
SWEEP SPEED – 20 msec/division
SCALE FACTOR – 4
AVERAGES – 100
ARTIFACT REJECTION – On

2. **Electrode montage**

ACTIVE – earlobe (ipsilateral) on the same side as the stimulus
REFERENCE – Vertex (Cz)
GROUND – earlobe on the opposite from the stimulus (contralateral) or Fpz

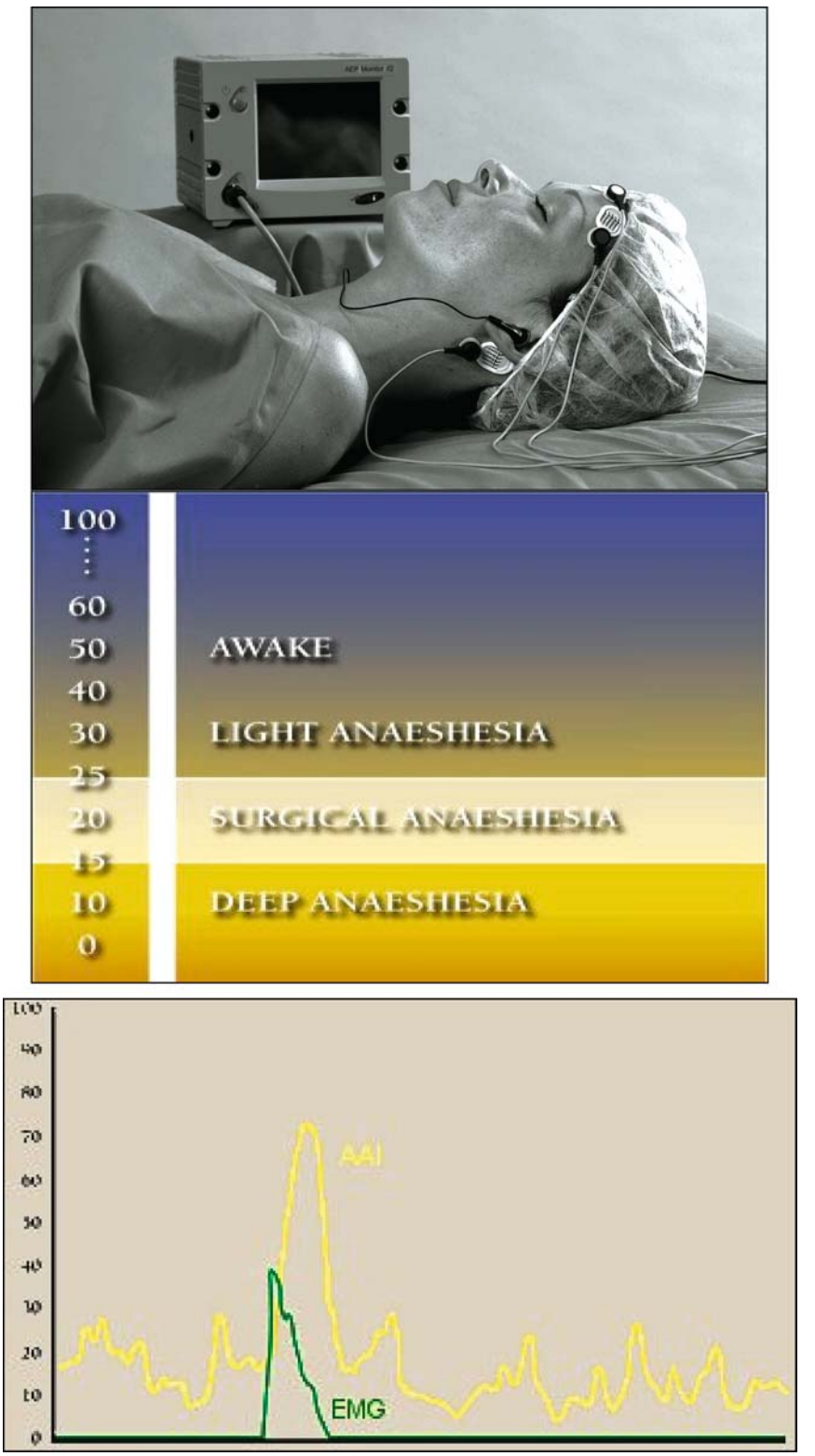


Fig. 85. Representative tracing of a patient during anesthesia where a sudden increase in nociceptive input results in lightening of anesthesia (increase in AAI-index) with increase of frontal muscle activity (EMG). Difference in response of the AAI- and the Bispectral-index (BS) shortly following an intravenous injection of the hypnotic propofol.

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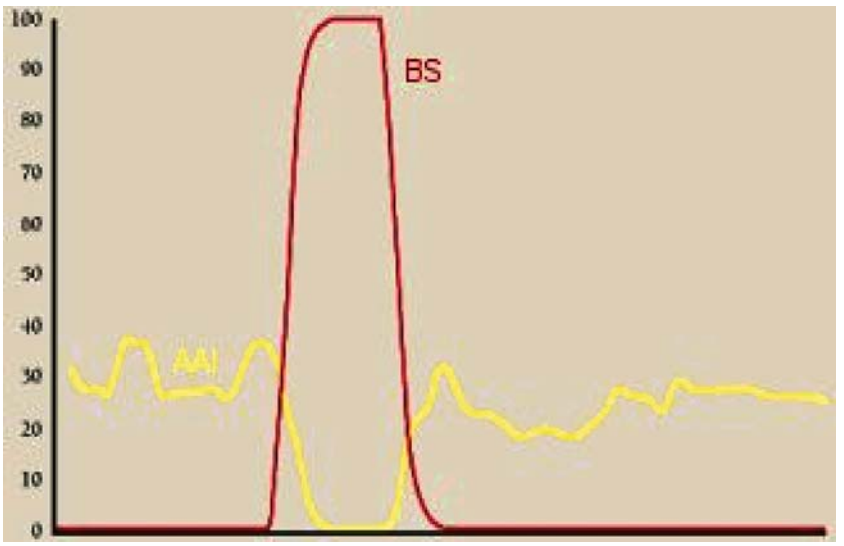


Fig. 85. (Continued)

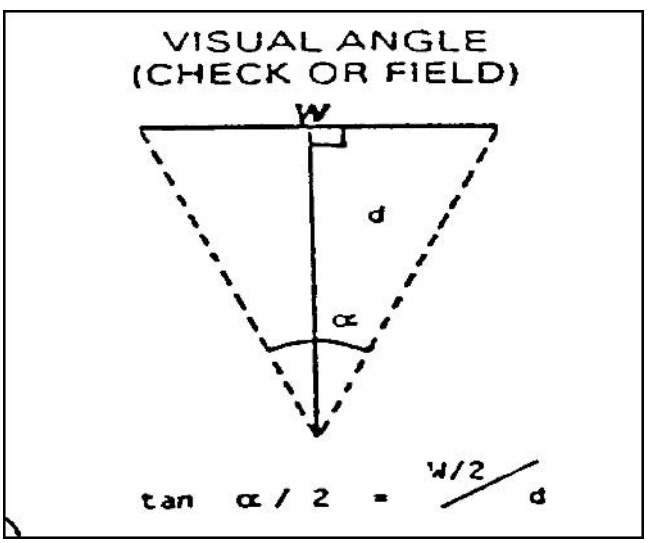


Fig. 86. Optimizing the angle in visual evoked potential recording using the reversal pattern check board on a TV screen.

Note: When the stimulus is switched from one ear to the other, ACTIVE and GROUND must also be reversed.

3. **Patient** – electrode montage

   ACTIVE: OZ′
   REFERENCE: Cz
   GROUND: Fpz

4. **Procedure**: Replicate the results twice, and evaluate the results for consistency.

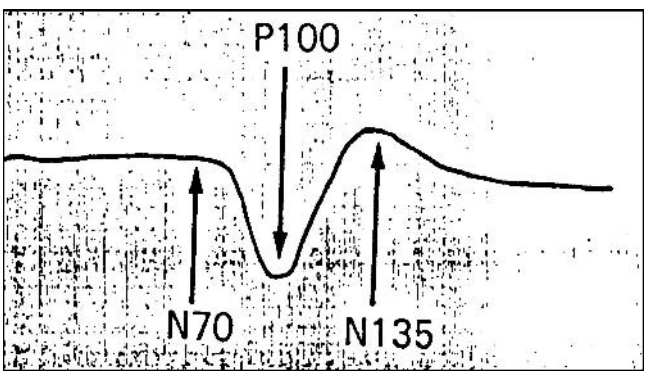


Fig. 87. The response waveform in VEPs, as they are derived from the occipital cortex.

If waveform is unclear, or for example, there is no response check for perception, use smaller or larger checks, and/or reduce ambient light sources. If there is too much noise in the reading, increase number of averages, use the 60-Hz notch filter, and/or increase the patient's relaxation status.

5. **Measurement of VEPs**
   Find the large P_{100} peak, which is the major reproducible peak showing a downward deflection (Figure 87).

Determine the absolute latencies of all waveform components, establish the difference between the P_{100} obtained from the left and right eye, and determine the amplitude height of the P_{100} peak. Also, establish the difference

Table 14. Normative values in VEPs where Abs = absolute value; L-R Diff = left to right difference; Amp L-R Diff = Amplitude height difference of left to right

	Mean	S.D.
Abs P-100	102.3	5.1
L-R+ Diff.	1.3	2.0
Amp P-100	10.1 μV	4.2 μV
Amp L-R Diff.	1.6 μV	1.4 μV
Duration	63	8.7
Duration Diff.	2.8	2.9

between the left and the right P_{100} amplitude height, evaluating the duration (latency) of the response and compute the difference between left and right P_{100} latency.

The normal values for above-mentioned parameters are shown in the following table. They are not to be used clinically to identify a pathology and should only be used as a guide (Table 14).

Factors, which alter the response in event-related visual nerve stimulation

Non-pathologic stimulus factors that can alter the response

1. The **luminance of stimulus**. Latency increases as luminance decrease showing a 15-msec/log-unit reduction and a 15% reduction in amplitude height.
2. If **contrast** decreases, latency increases and amplitude height decreases using to the following equation:

$$\frac{L_l - L_d}{L_l + L_d} = 100\%$$

3. The **field size**: If central field size is changed by 2°, there is a 12.5% change in P_{100} amplitude height. If however, the central field is changed by 8°, there already is an 80% change in P100 amplitude height. Any change in total field size by 15–32°, an additional 2% has to be added to the P_{100} amplitude. Also, note that there is an overall luminance increase in luminance with increase in field size.
4. The **check size**: There is maximal response to 15–30° check size, and larger (32°) check sizes will result in maximal 1° change. Changes to flash response are observed as check size increases.
5. **Reversal speed:** The P_{100} latency increases as reversal slows down. The LED gives response latencies approximately 5 msec shorter than that at television presentation.
6. **Repetition rate**. Latency increases as rate increases. For example, there is a 4.8 msec increase as rate goes from 1 to 4 Hz. A rate of 8–10 Hz merges to a steady-state response.
7. **Filter settings** is 5–70 Hz. The high-cut can go down as low as 100 Hz. Notify, that the notch filter for 60 Hz can alter the response. The low-cut filter should not be higher than 1 Hz as otherwise there is a decrease in latency by 10 msec if the low-cut filter is set at 10 Hz.

Non-pathologic subject factors that can alter the response

1. **Age**: The latency begins to increase above 60 years of age. As for infants, no conclusive data exists, except that latencies match adult measurements by 6 years of age.
2. **Acuity**: Amplitude decreases as acuity decreases. As long as luminance remains constant (observe for cataract), and large checks are used (using 1°), latency will not change.
3. **Body temperature**: Any fluctuations in body temperature does not cause significant changes.
4. **Gender differences**: Females have slightly shorter latencies than males (1.5 msec shorter).
5. **Sleep stages**: If the patient is drowsy, he will not be able to focus. Also, inattention causes loss of focus, which results in a decrease of amplitude.
6. **Medication**: There are few reports on the effects of VEP. For example, methylphenidate (a stimulant) has an effect, while lithium has no effect. A patient on a barbiturate derivative, w will not be able to focus.
7. In **anesthesia**, where LED are incorporated in goggles are used, first establish a base-line with steady-state anesthetic level as any change in anesthetic depth may affect latency and amplitude of VEPs.

Detecting a pathology when using VEPs

Full-field VEPs for the left and the right eye can detect and localize optic nerve pathology. However, an optic nerve to retinal distinction can only be obtained by means of the results using an electroretinogram (ERG). Post-chiasmal and chiasmal pathologies may be detected by using half-field VEP results.

Problems arising during VEP measurement

The response is not a simple one as it is the additive sum of all responses from the visual cortex. Also, responses from healthy nerve fibers can mask the response from unhealthy fibers. Visual field deficits can look like multiple sclerosis

Table 15. Check and field sizes for both TV and LED stimulators in VEP measurement

CHECK AND FIELD SIZE			
Patients distance to TV screen in cm	Small check size in minutes	Large check size in minutes	Field size in degrees
160	15	30	2.6
80	30	60	5.2
40	60	120	10.2

(MS). It therefore is mandatory not to over-read the results. Any increase in latency alone is not enough of a criterion; the morphology must also be considered when using the VEP waveform as a diagnostic tool.

Summary of settings when using pattern-reversal VEPs

Stimulus parameters

Rate – 2.11/sec
Patient distance – 80 cm
Check size – 30°
Field size – 5.2°

Intrument parameters

Gain – 20 μV/div
High-cut filter – 100 Hz
Low-ct filter – 1 Hz
Sweep speed – 25 msec/div (250 ms/epoch)
Scale factor – 2 or 4
Averages – 250
Artifact rejection – off

Electrode montage

ACTIVE – Oz, which is 2 $\frac{1}{2}$ cm above inion in midline
REFRENCE – Cz
GROUND – either earlobe or Fpz

Procedure for VEP recording

Check patients visual acuity with the Snellen card and seat him in a dimly lighted room with an alternating checkerboard screen situated 80 cm from the face, at eye level, Cover one eye with an eye patch and have the patient fixate on a point at the center of the screen.

Collect replicated responses and display the waveforms on the screen for evaluation and for reproducibility. Then identify the prominent peak (P_{100}) and measure the peak latencies and amplitudes. Compare the results with normal values and print out the waveform for record keeping.

The purpose of this type of evoked potential measurement is the non-invasive evaluation of the functional state of optic pathways between the retina and the visual cortex. It is useful in the search for organic evidence of a deficit. Thus, the VEP is helpful during operations, which in may impede the optic pathway to the occipital cortex such as:

(a) Hypophysectomy,
(b) Resection of retro-orbital lesions,
(c) Procedures involving the occipital cortex, and
(d) Epilepsy surgery.

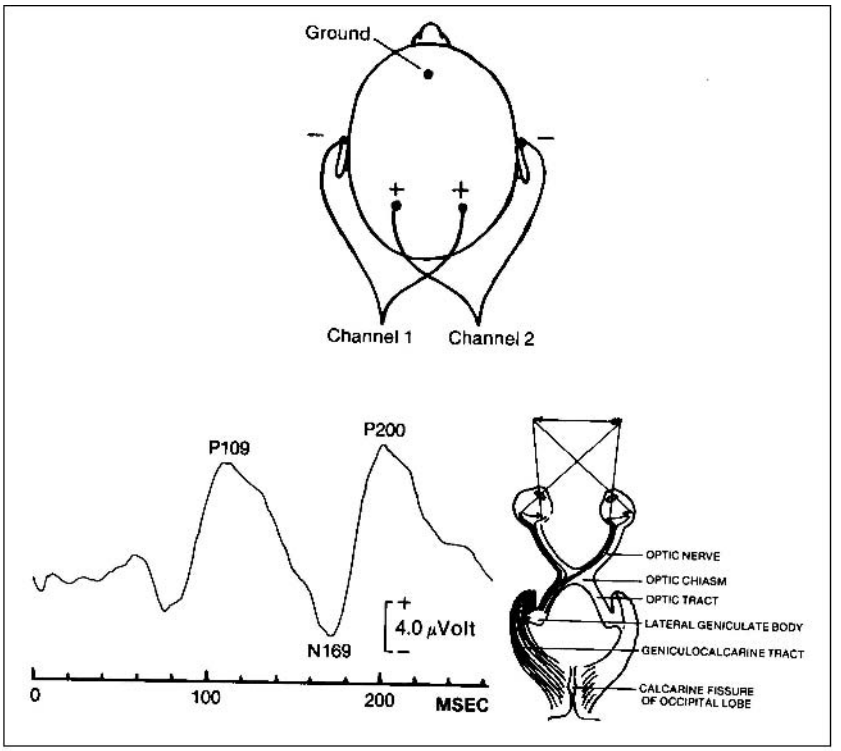
For stimulation of the visual sensory pathway a special flash-stimulus generator in a set of monocular or binocular goggles, which are placed over the patient's closed eyelids. The cortical function dictates that the majority of the visual cortex reflects foveal perception. The response waveform is recorded from the electrode positioning as demonstrated in the following figure.

Summary of technique for VEP monitoring

For event-related visual stimulation flashing light-emitting diodes (LED) or strobe lights are given, and potentials are recorded with scalp electrodes. In addition, signal-averaging and noise-reduction techniques are used. With an averaging rate of 100 sweeps, a stimulus rate of 2–11/s and a duration of 5 ms, two detectable major downward deflections named P_{100} and P_{200} are seen consistently. The proceeding N_{70} often is difficult to identify and the later N_{169} is inconsistent in its appearance. All waveforms are generated from the primary visual cortex, before higher association areas. No sub-cortical potentials have been found yet (Figure 88).

Interpretation of VEPs

Interpretation is typically done using the 3 negative peaks (N_{100}, N_{200}, N_{300}) and 3 positive peaks (P_{100}, P_{200}, P_{300}) are seen (Figure 89). During surgery the P_{100}-N_{200}-P_{200} complex typically is monitored including changes in latency and amplitude. In addition, VEP are commonly used in the diagnostic laboratory, since these responses are commonly used in the diagnosis of Multiple Sclerosis (MS), a relapsing and remitting condition, which is characterized by patchy inflammation affecting the myelin sheath of the central nervous system. The object is to demonstrate abnormalities in all regions of the nervous system not known from clinical manifestations to be involved, the silent lesions. For example, the finding of abnormal VEPs or BAEPs in a patient with paraparesis would demonstrate



Recording parameters	Stimulation parameters
Channel 1: $O_2 - A_1$ Channel 2: $O_1 - A_2$ Ground: FpZ Filters, 1 – 100 Hz Sensitivity: ±50 μVolt (full scale) Sweep time: 262 msec Sampling rate: 39806 Hz Repetitions: 128	Pattern reversal checker board on TV-screen reversed every 20-30 ms or light emitting diodes Stimulus: 2 – 11 Hz Duration: 5 ms Averaging rate: 100 sweeps

Fig. 88. Electrode montage, recording and stimulation parameters during visual evoked potential monitoring using monocular or binocular goggles.

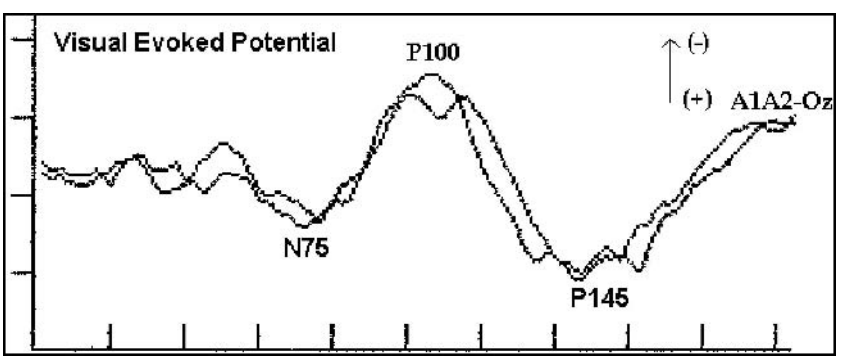


Fig. 89. Typical VEP waveforms as they are recorded from the occipital cortex.

abnormalities in at least 2 sites of the central nervous system, a characteristical trait of MS.

Optic nerve alterations can only be separated from retinal abnormalities by means of the ERG (electroretinogram), an additional visual electrodiagnostic system. Post-chiasmal and chiasmal pathologies may only be detected by half-field VEP, while the full field VEP can localize optic nerve pathology. The response during VEP is not easy to read as it represents the additive sum of all responses from the visual cortex. Thus, responses from healthy nerve fibers may mask responses from unhealthy fibers. As some visual field deficits look like multiple sclerosis, one should not over-read the results when interpreting an increase in latency. One has to consider the morphology as well. Another problem stems from the opaque goggles used for emitting flash signals. The goggle housing should be well supported by the bony ridge of the orbit, as it inadvertently may slip into a position resulting into direct pressure on the globe of the eye, which may cause central retinal artery thrombosis.

Preclinical specifications for intraoperative VEP monitoring include stimulus rate, electrode location, or filter setting have not yet been fully defined. As most of the currently used anesthetic techniques induce small pupils, the reliability of monitoring may be hampered. And since intraoperative VEPs are extremely sensitive to the effects of anesthetic agents [43], amplitude and latency changes may be related to the anesthetic affect, which is because intraoperative VEP monitoring is of little value. Postoperatively, however, besides detecting alterations, VEPs correlate well with improvement in vision after operation [2], and intraoperative irreversible VEP changes were found to go hand-in-hand with postoperative decreased visual function or an intractable intracranial hypertension [44].

VEP measurements in the OR is indicated whenever a potential deterioration in the visual pathway might ensue during the following surgical procedure:

1. Hypophysectomy
2. Retroorbital surgery
3. Occipital cortical surgery
4. Lateral ventro-cerebellar lesions

In order to determine a possible lesion, the following parameters should be used during routine VEP measurements:

(a) Difference in latency of the P_{100} obtained from the left and right eye respectively.
(b) Determination of difference in amplitude height of the P_{200} from the left and right eye respectively.
(c) Determination of absolute latency of all waveform components.

Usually, as in the other modalities of evoked potential measurements, results should be replicated twice and evaluated for consistency. If the waveform, however, tends to be unclear:

(a) The ambient light source is to be reduced since any decrease in light contrast results in an increase in latency and a decrease of amplitude.
(b) Reduce ambient noise by increasing the number of averages, or increase the relaxation of the patient, or use a 60 Hz notch filter.
(c) Since replication rate of the foveal stimulation has some impact on waveform configuration, an increase of stimulation from 1–4 Hz results in an increase in latency up to 45 ms. A rate between 8–10 Hz, however, merges to a steady-state response.

Investigators who initially were enthusiastic about the value of intraoperative VEP monitoring, however, are somewhat disillusioned. This is because there are a number of technical problems continue to limit the usefulness of VEPs. The flash evoked potentials elicited by light-emitting diodes mounted in opaque goggles are less well defined and less reproducible than the pattern reversal checkerboard evoked potential (PREP) which is used in the diagnostic laboratory. In the latter the individual has to sit in front of a TV screen focusing on checkerboard pattern, which is reversed every 20–30 ms in regard to black and white contours (pattern reversal stimulus generator; Figure 90).

The disillusion in the use of VEPs in the operation room stems from experiences described in the literature, which regard the clinical utility of intraoperative VEP as conflicting. Monitoring has been performed in tumor resections that require manipulation of the optic apparatus, but its use has not yet become standard practice. The method currently provides the most sensitive technique in detecting subclinical lesions of the optic nerve (Figure 91) and may enable a diagnosis of multiple sclerosis to be made at an earlier time than with SSEPs. Abnormalities in the VEP are also encountered with compressive lesions of the anterior visual pathways. In pediatry, the flash VEP may be used as a screening test of the visual pathway.

Monitoring of visual pathways therefore has potential utility in surgery performed in proximity to the visual apparatus, especially in the parasellar region. Tumors that arise in this area include craniopharyngiomas, pituitary adenomas, and suprasellar meningiomas. Since resection of these tumors carries significant risk of visual impairment, VEPs have been performed successfully to aid in the monitoring of visual function during surgery in the hope of detecting visual impairment before it is irreversible. It has potential

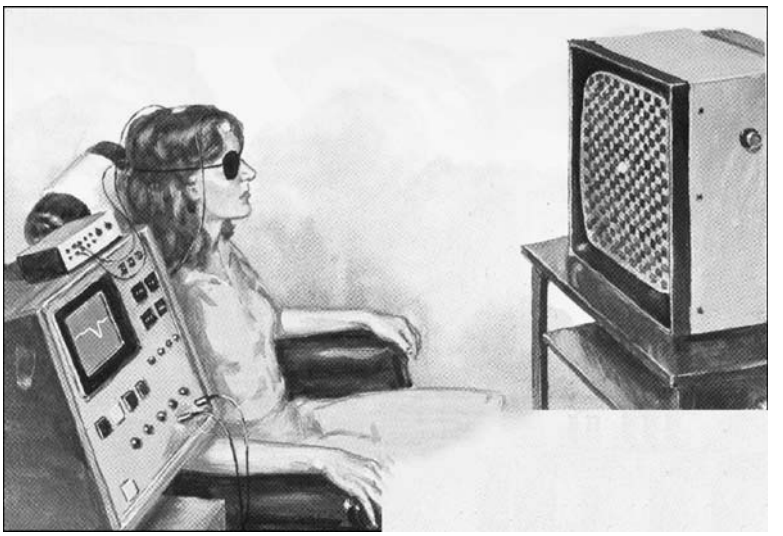


Fig. 90. The visual evoked potential being induced by a changing checker board pattern.

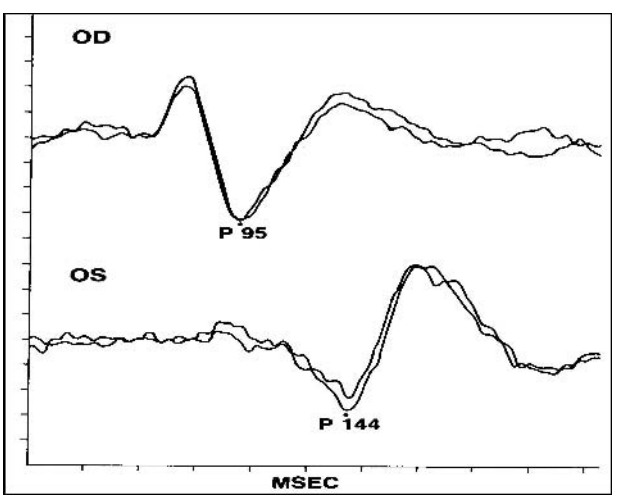


Fig. 91. Comparative VEP of the right (OD) to the left (OS) demonstrating neuritis with latency increase of the left eye using following specifications: latency = 25 ms/division; amplitude = 2.5 μV/division.

usefulness in assessing integrity of visual pathway structures including optic nerves. Because intraoperative use of VEPs is still in its infancy and further work is required to determine its full clinical utility.

The VEP is not able to detect the presence of visual field defects.

Complications that can arise during EP monitoring

Risk of electrophysiological monitoring of the nervous system is minimal and may be compared to the risk of recording an ECG. Observing the standard procedures of care when using electrical devices minimizes hazards of burn when patients are attached to multiple electrical devices. Any leakage of current from the monitor to the patient should be less than 10 μA, and from the monitor to its case less than 100 μA. It is of importance to make sure that all electrical devices attached to the patient derive their power from single insulation grounding. One has to keep in mind the possibility of pressure necrosis whenever electrodes are attached percutaneously to comatose or anesthetized patients over a longer period. Especially during VEP monitoring, care has to be taken to avoid pressure from the goggles used to emit flash stimuli.

Last but not least one should be aware of collecting erroneous data due to equipment failure or due to errors in methodology, technical difficulties, or inexperienced personnel. The frequency at which wrong data are collected seems to be inversely related to the experience of the team and, the degree of meticulous attention to technical details of recording and interpretation. Although the complexity of electrophysiological monitoring in some institutions may reach the boundaries, difficulties encountered in many ways reflect those seen typically during the early days of ECG recording. Some of the systems on the market today which are able to record all modalities of evoked potentials are too bulky, expensive, and not easy to operate. However, the scene is slowly changing as more and more systems get

less expensive, incorporate less cumbersome technique, are more compact and flexible, thus opening a new world of monitoring for the clinician.

One shortcoming in EP monitoring is not that of equipment, but that of lack of experienced personnel, which is trained in recording and interpreting EPs in the OR and in the intensive care unit. While an EEG technician should be available in the institution for electrode montage, for the meticulous attention of electrode setting as well as data acquisition, the physician is responsible for data interpretation. As the interpretation of EP waveform rests primarily on pattern recognition, EP changes have to be looked at in the light of all pharmacological and pathophysiological changes.

Regardless of the physician's specialization, the individual involved with the interpretation of EPs would have to gain additional knowledge in an area outside his or her specialty. The skill in EP interpretation in the OR and/or the ICU is in direct proportion to the individual's degree of interest and experience in this new neurophysiological methodology.

TAKING CARE OF ELECTRODES – RE-SILVERCHLORIDING

The silver/silver chloride stick-on electrodes are manufactured of pure silver with their surfaces chlorided. They are of circular shape, have a domed top with a small hole in the center, suitable for the application of electrode jelly. A highly flexible PVC-covered cable is attached to the electrode by a crimp connection. Shrink sleeving covers the joint. Many EEG users could get better results if only a little more attention was given to the care of such electrodes. First and foremost, one must appreciate that electrodes are reusable but have a limited useful lifetime. Nevertheless, their life can be prolonged and their performance considerably improved if the users allow themselves time to prepare used electrodes. Although claims are made for various metals, or plated metals, giving superior EEG and SEP recording performances, up to this date it is the general opinion of the leaders in EEG recording that silver/silver chloride electrodes, when carefully looked after, are difficult to improve upon. The EEG and EP electrodes commonly used in Europe and the US are made from pure silver and coated with silver chloride. Such an electrode acts as a reversible chloride electrode and with care can be re-chlorided easily. The following incorporates some simple hints on the preparation of silver/silver chloride electrodes (Figure 92).

Preparation is much more complex as outlined below; for further information textbooks or publications on practical physical chemistry or electro-chemistry should be consulted.

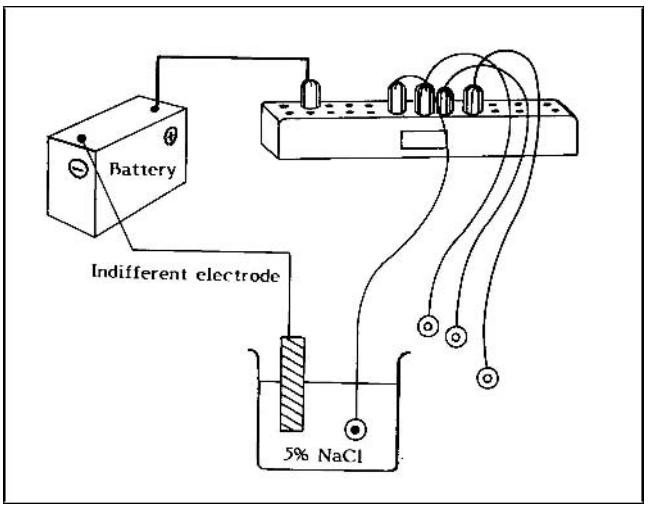


Fig. 92. Methodology for re-silver-chloriding stick-on electrodes.

1. Use only pure silver.
2. Clean silver before chloriding with an abrasive such as sand paper, or abrasive paste, e.g., jeweler's rouge, but not steel wool or a file, because this can lead to a contamination of the silver with iron.
3. Chloride at a rate of 2.5 mA/sq.cm for several minutes in bromide free sodium chloride solution. The strength of the solution is not critical, but at least physiological saline, and up to 5% concentration should be used. Contrary to general belief, the properties of the chloride layer are not changed by exposure to light. After preparation, the electrodes will show potential differences, which may amount to tens of millivolt or even more in some cases.
4. If the electrodes are stored in saline or externally shortened together these potentials can be discharged, but when disconnected or in use, some of the potentials return over a period of minutes or hours. Thus, slow drift is of little consequence if AC-coupled amplifiers are used (i.e. the normal EEG amplifier), but it is of great inconvenience if DC recording is required. The figure shows a suitable method to silver chloride a used set of stick-on electrodes. They should be cleaned of old chloride with a suitable non-metallic abrasive paste, or a similar scouring powder, washed clean under cold water, and then ideally electrolytically cleaned by reverse silver chloriding at about 20–30 Volts DC, i.e. the recording electrode is made negative by about 20 Volts DC with respect to an indifferent electrode for a few seconds. All stick-on electrodes then are connected to the positive terminal of a 1.5–2.0 Volt battery. The indifferent electrode may be a piece of silver, or carbon, and is connected to the negative terminal.

5. The electrolyte solution is 5% NaCl and, once used for this purpose, must be discarded. Each electrode is lowered into the saline solution for approximately one minute. It will be seen that the original bright, silver-colored electrode turns into a dark violet color when fully silver-chlorided. EEG electrodes perform best when they are equipotent with respect to each other, and remain so even though currents are passing into them and out again. This equipotency is only possible when they are silver-chlorided. Re-chloriding is necessary after 30–60 recordings. In practice, even when the electrode looks clean as though all silver chloride was rubbed off, it will still perform well. It is difficult to get electrodes looking evenly coated with silver chloride after they have been used, and although they look mottled and patchy, nevertheless they record quite adequately.
6. Needle electrodes are made of hard metal. Platinum is for sub-dermal, and stainless steel for sphenoid recording. These metals polarize resulting in different resistances. The main reason why the needle electrodes did not become number one in EEG and EP recording is that they have to be autoclaved in order to avoid infection. Normal plastic insulation does not withstand to continuous autoclaving, so these electrodes are considered as unreliable and expensive by most laboratories.

SUMMARY OF THE CLINICAL APPLICATION OF EVOKED POTENTIAL MONITORING IN THE OR

The range of applications for sensory evoked potentials is growing, as demonstrated in several reviews [2, 43]. Evoked potential monitoring indicates when something is altering the neural pathways, provided that the effect of anesthetics, temperature, and arterial pressure can be excluded as causes. Visual evoked potential monitoring, which may present a useful technique in operations involving the optic nerve and the chiasma, however, has not had the expected success in application. This is mainly due to the difficulty in delivering a stimulus during surgery. Firstly, unshielded flashing of a stroboscope is distracting to the surgeon, and light-emitting diodes mounted in goggles are not a universal effective stimulus. Secondly, there is the problem of inherent variability of potentials, and thirdly, there is the depressant effect of anesthetics. The variability of the potentials and the inaccuracy of the results do not justify routine VEP monitoring. Monitoring of auditory brainstem evoked potentials (BAEP) has a much greater success, especially in posterior fossa procedures [44]. Most common applications of somatosensory evoked potential testing (SSEP) are operations for scoliosis and related disorders, as well as neurosurgical and vascular procedures. The area of controversy is the choice between spinal and cortical recording. While spinal recording involves the disadvantage of needing epidural electrodes for high-quality recording and the problem of multiple pathways being stimulated, cortical recording has the advantage of being non-invasive. The EPs of cortical recording are, however, greatly influenced by hypotension and anesthesia. The recently described technique of transcranial stimulation of motor pathways and the recording of large descending spinal pathways via esophageal electrodes present an extension of this methodology [45]. Clear-cut indications where SSEP monitoring is used beneficially are:

- Traumatized lesions of the brachial plexus;
- Aneurysms of the descending aorta with extensive replants by grafts. This incorporates occlusion of the aorta and hence interruption of the anterior spinal cord supply via intercostal vessels. Time limits for loss of sensory evoked potentials can thus be defined. Additionally, those arteries necessary for nervous function, after re-implantation result in a recovery of the depressed signal, can thus be defined. However, whether the SSEPs are representative for the more important motor pathways remains to be seen;
- During carotid endarterectomy (CEA), EEG monitoring in this respect has some limitations in that an infarction of the middle cerebral artery may result in ischemia of subcortical layers. Thus, warning signs are better derived from evoked potentials, which have to travel through the area of ischemia. The EEG will only detect ischemia of the cortical layers;
- Continuous EEG – with interlapped SSEP monitoring which nowadays seems sensible to use as a combined approach. If the signal of SSEP averaging plus EEG recording and processing deteriorates against a baseline at the moment of clamping, it would mean the indication for by-pass shunting;
- In cardiac surgery where marked hypothermia presents a problem as cooling may mask ischemia. In view of the lower vulnerability of the brain stem than the cortex to ischemia, BAEP are inappropriate for an early warning signal. The short latency SSEP remains the most valuable in this respect. Peaks tend to be attenuated if temperature drops below 25–20 °C – during controlled hypotension as it is used in the case of operating upon an intracranial aneurysm. SSEPs serve as an early warning signal of ischemia in which central conduction time (CCT) shows a close correlation to pressure, especially when the blood flow drops below 30 ml/100 g/min [46].

WHEN TO USE WHAT EVOKED POTENTIAL MODALITY?

Auditory evoked potentials (AEP) brainstem auditory evoked potentials (BAEP):

- Acoustic neuroma resection
- Posterior fossa operations
- Diagnosis of brain stem damage.

Intermediate and long-latency Auditory Evoked Potentials:

- Resection of temporal-parietal lesions
- Epilepsy surgery
- Localization of the specific auditory cortex

Somatosensory Evoked Potentials (SEP)
Short-latency Somatosensory Evoked Potential (SSEP):

- Identification of peripheral nerve lesions and resections
- Identification of spinal cord lesions
- Operative treatment of scoliosis (for instance Harrington rod insertion and removal, spinal fusion)
- Brain stem damage

Intermediate and long-latency Somatosensory Evoked Potentials (SSEP):

- Intracerebral aneurysm clipping
- Indicator of hypoxemia, malperfusion
- Effect of central active drugs
- Efficacy of central analgesics
- Prognostic value and efficacy of treatment in head trauma
- Intracerebral bleeding
- Epilepsy surgery
- Stereotactic thalamic procedures
- Resection of parietal lesions in neurosurgery
- Posterior fossa procedures

Visual Evoked Potentials (VEP)

- Hypophysectomy
- Resection of retro-orbital lesions
- Operative procedures involving the occipital cortex

Summary of the clinical application of EP monitoring in the ICU

Evoked potential abnormalities have to be interpreted in the light of whether or not they represent a transient dysfunction or a permanent damage. This is the main reason for serial recording of SSEPs in the ICU in order to observe trends.

Somatosensory evoked potentials are especially valuable in determining the mechanisms of coma. When serial recording shows a lack of cortical components but a preservation of waves generated in the spine and the brain stem, cortical lesions have to be suspected. When cortical potentials are visible, central conduction time (CCT) presents a good prognostic indicator. It is markedly prolonged in patients after head injury, less in non-traumatic patients. A gradual return of CCT to normal ranges in patients with traumatic coma reflects the rate and the degree of improvement being independent of temperature changes between 35–38 °C. Short-latency sensory evoked potentials are not affected by massive doses of sedatives. Thus, normal brain stem evoked potentials in a patient with isoelectric EEG, areflexy, and apnoe suggests drug overdose. The presence of normal or near normal short-latency somatosensory evoked potentials in patients with an iatrogenic depressed EEG and motor reflex (such as it may be seen in high dose barbiturate or benzodiazepine overdose with cumulative effects) offers the likelihood of recovery. Poor quality outcome in patients after head injury or a raised intracranial pressure is preceded by incomplete recovery of later cortical components. They, however, return to normal in patients making satisfactory improvement. Thus, SSEPs per se give an early guide to the recovery of head-injured patients. Those with sustained absence of early-evoked somatosensory potentials of the right and the left side will not recover. Those with marked asymmetry or severe abnormality of the peak are at best capable of survival with severe damage or in a vegetative state. Those with minor short-latency asymmetries or morphological abnormalities of the wave eventually will recover fully even in spite of the early neurological deficits. The combined use of the EEG and the evoked potential (EP) gives greater accuracy to predict outcome than would be achieved with either test alone. Such a combination helps to overcome problems of interpretation of clinical data even in the presence of high levels of sedative drugs. Additionally, in the isoelectric EEG after cardiac arrest with persistent cortical evoked potentials this can be a monitoring sign of later recovery when compared to cases with isoelectric EEG and an absent cortical EP. In the latter, neocortical death is likely if cortical components and/or short latency components show sustained absence [47]. Although brain-stem auditory evoked potentials (BAEP) are helpful in confirming brain death, some institutions believe the somatosensory evoked potentials (SSEP) to be of greater clinical usefulness in the setting of brain death. This assumption is born out of the observation, that it is important to have an input signal suggesting the arrival 01 the stimulus to the central nervous system. Such a differentiation is not that easy when using brain stem auditory evoked potentials [48]. No brain death patients do show absent late components. Comatose patients with

preserved brain-stem function, however, present a range of abnormalities, which correlate with the neuropathological finding. It, however, has to be born in mind, that the causes of evoked potential abnormalities may also be within a reversible toxic, or hypothermic origin. Thus, it seems wise not to make a vital decision on the basis of absent potentials and emphasize waves, and potentials that are present.

GLOSSARY

Common abbreviations and definitions used in clinical electrophysiology (in alphabetical order)

AAI	anesthesia awareness index
AC	alternating current
AE	activity edge
AEP	auditory evoked potential
AP	action potential
BAEP	brainstem auditory evoked potential
BAER	brainstem auditory evoked response
BEAM	brain electrical activity mapping
BIS	bispectral index
CBF	cerebral blood flow
CCT	central conduction time
CDSA	color density spectral array
CEA	carotid endarterectomy
CNG	cochlear nystagmogram
CNS	central nervous system
CSA	continuous, compressed spectral array
CSI	cerebral state indices
CSM	cerebral state monitor
CV	conduction velocity
DC	direct current
DSA	density modulated spectral array
ECochG	electrocochleogram
EEG	electroencephalogram or electroencephalograph
EMG	electromyogram
ENG	electronystagmogram
EOG	electrooculogram
EPSP	excitatory postsynaptic potential
EP	evoked potential, also Erb's point when used in illustrations
ERA	evoked response audiometry
ERG	electroretinogram
Far-field potentials	Potentials that arise at sites distant from the recording electrode
FED	flash emitting diodes
FEP	flash evoked potential
FEMG	frontal electromyogram, frontalis electromyography
FFT	fast Fourier Transform
Fp	fossa popliteal
High frequency filter	an electronic filter that permits only pass of lower frequencies
Hz	Hertz
IPSP	inhibitory postsynaptic potential
JvO2	mixed venous bulbular oxygen tension
LED	light emitting diodes
LMN	left median nerve
Low frequency filter	an electronic filter that permits only pass of high frequencies
LPTN	left posterior tibial nerve
MEP	motor evoked potential
ML-AEP	middle Latency AEP
MTA	moving time average method
MPF	median power frequency
Near-field potentials	Potentials passing immediately below the recording electrode
PA	paradoxical arousal
PPF	peak power frequency
PSA	patient state analyzer
PSI	patient state index
RE	response entropy
RMN	right median nerve
RPTN	right posterior tibial nerve
SAEP	short latency auditory evoked potential
SEP	somatosensory evoked potential
SE	state entropy
SpEP	spinal evoked potential
SSEP	short latency somatosensory evoked potential
SEF	spectral edge frequency
SFx	spectral frequency index
VEP	visual evoked potential
VER	visual evoked response

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CEREBRAL MONITORING IN THE OPERATING ROOM AND THE INTENSIVE CARE UNIT: AN INTRODUCTORY FOR THE CLINICIAN AND A GUIDE FOR THE NOVICE WANTING TO OPEN A WINDOW TO THE BRAIN

Enno Freye

PART III: SPINAL CORD EVOKED POTENTIALS

Author address: Clinics of Vascular Surgery and Renal Transplantation, Heinrich-Heiue-University, Düsseldorf, Deichstr.3a 41468 Neuss-Uedesheim, Germany.
E-mail: enno.freye @uni-dusseldorf.de

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INTRODUCTION

Intraoperative spinal cord monitoring should provide reliable information to the surgeon at a critical scene during the operation affecting the spinal cord in way or the other and assist him/her to carry out aggressive surgery if necessary. This may either be a diseases of the spine, the spinal cord, or those vessels directly supplying the spinal cord. SSEPs (somatosensory cortical evoked potential) and the "wake up test" under neuroleptanesthesia will not be inc1uded in this chapter because of their imperfections to provide reliable information in the electrically hostile operating room and the shortcoming in providing continuous monitoring respectively. Since spinal cord ischemia during thoracoabdominal aneurysm (TAA) repair can result from arotic cross clamping and an insufficient restoration of blood flow thereafter have been subjects of several experimental and clinical studies where ischemic tolerance was prolonged by protection with various agents, including Ca^{++}-channel blockers, superoxide dismutase, prostaglandin E_1 (Figure 1) or prostacyclins respectively [1, 2].

Also, surgical techniques have been used to restore blood flow to the spinal cord thereby reducing the incidence of postoperative paraparesis or paraplegia. Among them are retrograde perfusion of oxygenated blood into intercostal arteries, the use of local hypothermia of the spinal cord, cerebrospinal fluid drainage, increase in perfusion pressure or left-sided heart by-pass surgery (3) However, in order to react to an endangered spinal cord it is necessary to monitor its function, and while the motor pathways in the anterior horn are more sensitive to ischemia than the dorsal horn, studies have demonstrated the usefulness of a selective monitoring of SCEPs (spinal cord evoked potentials) at the dorsal horn. This is because they can be used as an indicator for the surgeon as when to react and institute preventive measurements in order not to further jeopardize spinal cord function [1].

NEUROPHYSIOLOGIC METHODS UTILIZED IN THE OPERATING ROOM

To carry out continuous monitoring of the spinal cord function through the course of surgery neurophysiologic techniques are being utilized. The value of these techniques lies in early recognition of spinal cord dysfunction before it may become permanent and while it still is possible to undertake immediate measures for prevention. Techniques for monitoring long tracts in the spinal cord are well established

and regarded to be reliable to protect major spinal cord insult during the surgery of the spine and spinal cord [4–9]. However, there are reports of false negative cases [10, 11]. Also, there are a great number of unreported false positive cases. In order to eliminate these false results, selective sensory monitoring of those areas within the spine is done, i.e. applying the stimulus close to and recording the evoked response from an area close to the spinal cord, thus avoiding a possible effect of anesthesia, temperature changes and/or electrical noise within and outside the patient (Figure 2).

The electrical signals when derived for spinal cord monitoring, are divided into two groups:

1. Those mainly reflecting the activity of sensory tracts and
2. Those used to monitor the motor related tracts.

In the present chapter features and methods of recording of sensory-evoked potentials will be presented since motor-evoked potentials show two major disadvantages. First and most of all, they are significantly affected by different levels in anesthesia. It therefore is mandatory to closely cooperate with the anesthesiologist and make sure that there is a very constant level in the anesthesia plane. Secondly, all a muscle relaxants have a marked impact on the MEP (motor evoked potential) response. Therefore not only has the level of muscle relaxation to be monitored continuously, at the same time this level should be stable during the whole recording process as not to interfere with the recorded signal.

METHODS MAINLY REFLECTING THE ACTIVITY OF SENSORY TRACTS

Spinal cord evoked potentials (SCEPs) after stimulating the spinal cord have first been used independently by Tamaki

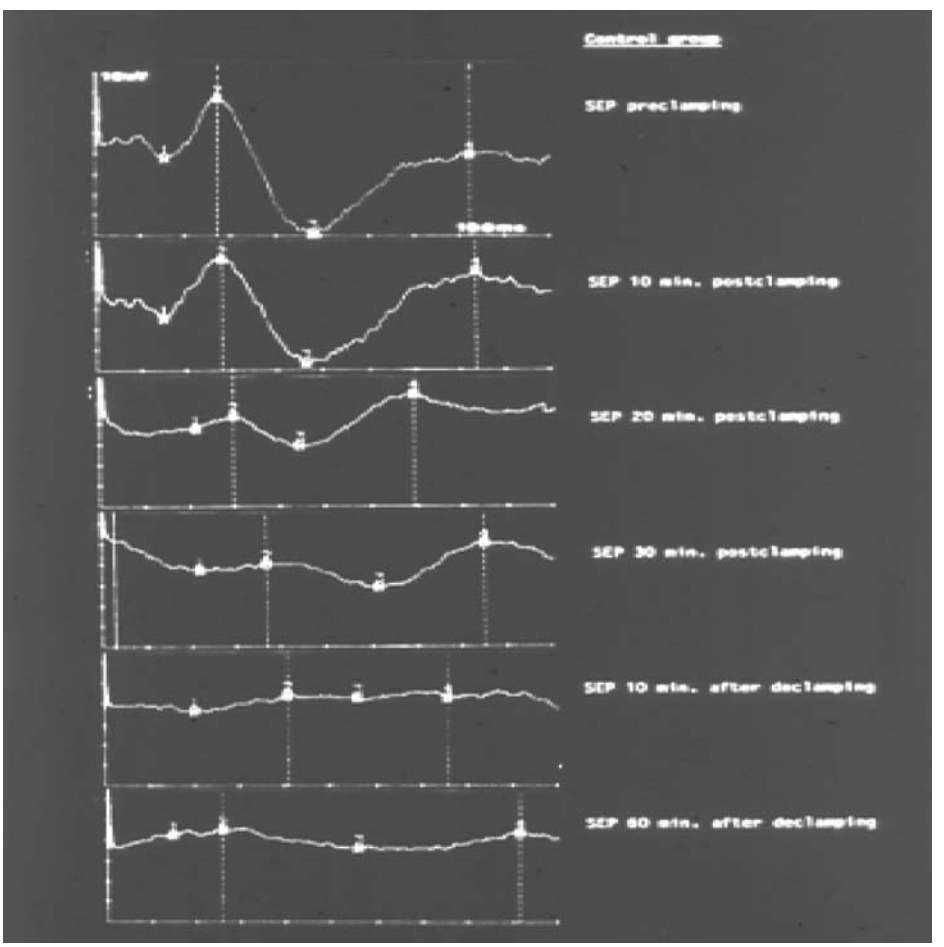

Fig. 1. Representative example of SCEPs in the canine. Compared to control prostaglandin infusion (PGE_{15} ng/kg /min) results in a complete recovery of the evoked potential following aortic cross clamping for 60 minutes. Adapted from [3].

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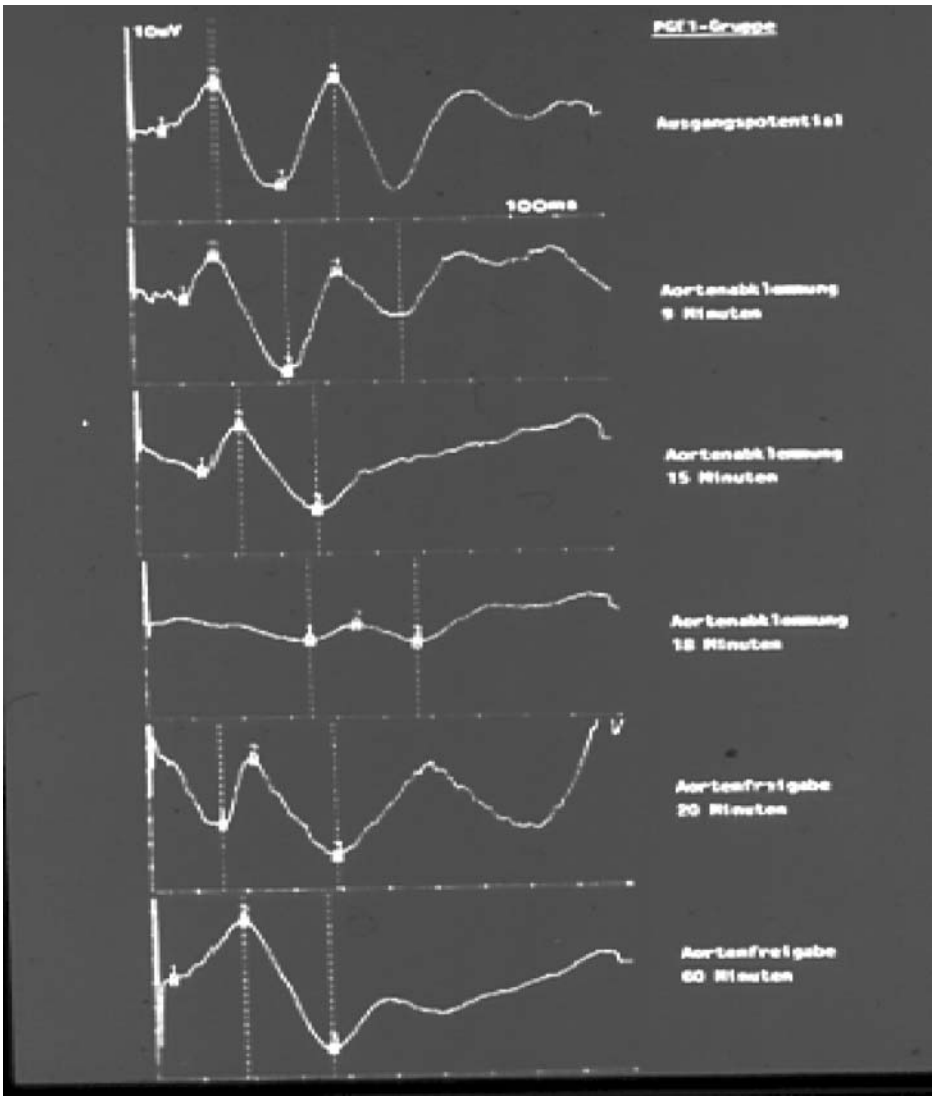

Fig. 1. (Continued)

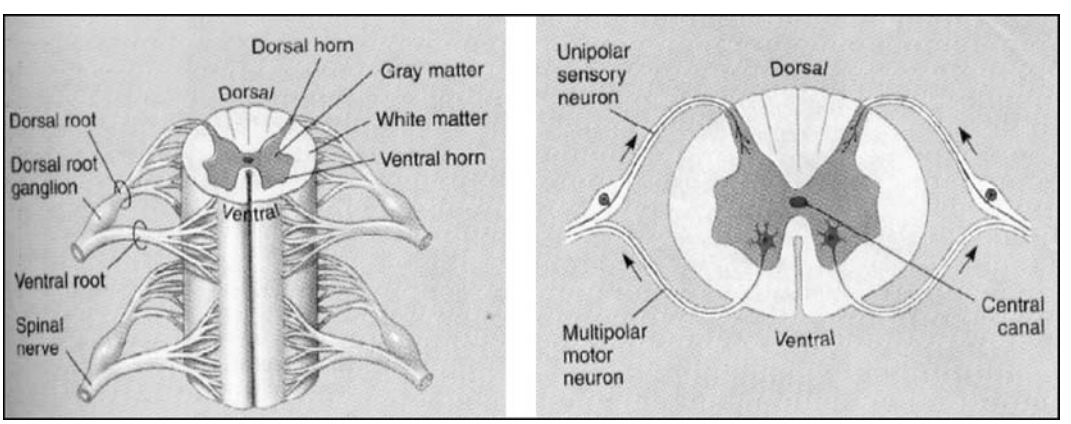

Fig. 2. Anatomy of the spinal cord with its relevant tracts, endangered in aortic cross clamping, which can be monitored with SCEPs.

and coworkers [12] and Kurokawa and associates [13] for the purpose to examine the continuity of long tracts in the spinal cord in independently. These author delivered a stimulus to the spinal cord at the rostral site and recorded the signal from a caudal site [8, 12] while Kurokawa recorded ascending volleys placing the recording electrode rostrally after stimulating at a caudal site of the spinal cord [9, 13]. There was no essential difference between the recorded SCEPs. The initial spike shape potential (first component) has been considered to represent the electrical activities originating from the large diameter nerve fibers located in the posterior-lateral region of the spinal cord by many investigators [14, 15] or by nerve fibers in all quadrants of the spinal cord by others [14, 16]. The succeeding polyphasic component (second component) has been regarded to reflect the continuity of the dorsal column [17]. Several other researchers [16, 18] have indicated the contribution of post-synaptically transmitted potentials to this part of the signal. Since the contribution of post-synaptic electrical activities is small in size, the SCEP is regarded mainly to reflect the activity of sensory related tracts. Such SCEPs differ from stimulation of peripheral nerve tracts. A group at the Royal National Orthopedic Hospital of England first described this latter type of evoked potential for intra-operative spinal cord monitoring [6]. They delivered electric stimulation to the tibial or the peroneal nerve trunk on both sides simultaneously and recorded signals from the spinal cord placing the recording electrode in the epidural space rostally to the site at risk. The SCEPs derived with this technique is composed of polyphasic waves and mainly reflects the conductivity of the dorsal column. If the stimulation is performed on one side, injuries lateral to this site of the spinal cord may be derived with this method. Segmental SCEP recording is possible with the recording electrode placed at the site of entry of impulses to the spinal cord. This method can be employed to monitor for instance the function of the conus medullaris.

On the other hand patients undergoing thoracoabdominal aortic aneurysm (TAA) reconstruction during which the aorta has to be clamped for 30 to 60 minutes by the vascular surgeon, postoperative paraplegia presents a major problem.

This is because aortic cross clamping results in an interruption of blood supply to the spinal cord from the intercostal arteries [20, 21] where perfusion of the spinal cord via the Adamkewicz artery is endangered (Figure 4). Depending on the type of aneurysm (Figure 3) there is a high percentage of patients who end up with either having paraparesis or paraplegia following operative correction of a thoracoabdominal aortic aneurysm (TAA). With an incidence in poor neurological outcome ranging from 10%–40% [21–23], it is necessary to give the surgeon a tool at hand, which indicates:

(1) Possible early functional loss of the spinal cord following cross clamping so he can take preventive measures,
(2) Alert the clinician of a potential postoperative motor deficit in the reperfusion period following declamping, and
(3) Point out the time of recovery of the evoked potential following declamping.

Especially, the time of recovery of SCEPs in the post declamping period is an important indicator, since it points toward the successful reimplantation of an intercostal artery composing the A. radicularis magna (Figure 4), which is necessary for spinal cord perfusion and has been shown to correlate closely with late motor function [24].

Since it is impossible to predict what aortic clamping time can be tolerated in a particular patient because the exact vascular anatomy, including collateral vessels that provide the spinal cord with blood, is unknown at this time. This explains why paraplegia might occur only after 30 minutes of aortic cross clamping in same patients and may not be present even after 60 minutes in others.

TECHNIQUES TO OBTAIN SCEPS AND MEPS

For the purpose of recording SCEPs, one has to arrange the stimulating and the recording electrodes with regard to the spinal cord segment of interest, the character of the anticipated injury to the spinal cord and the type of function modality to monitor. In other words, impulses provoked by the stimulation should be recorded after traveling through neural structures at risk so that their amplitudes and latencies reflect possible dysfunction. Furthermore, every effort to facilitate prompt recognition and response should be carried out.

PLACEMENT OF STIMULATION AND RECORDING ELECTRODE IN SCEPS

For stimulation and recording of SCEPs, flexible bipolar Bipacing-Cath® stimulation catheters are introduced into the subarachnoid space at level L4/5 and level Th7/8 respectively (Figure 5). This electrode consists of two helical platinum wires of 1 mm width attached to the end of a

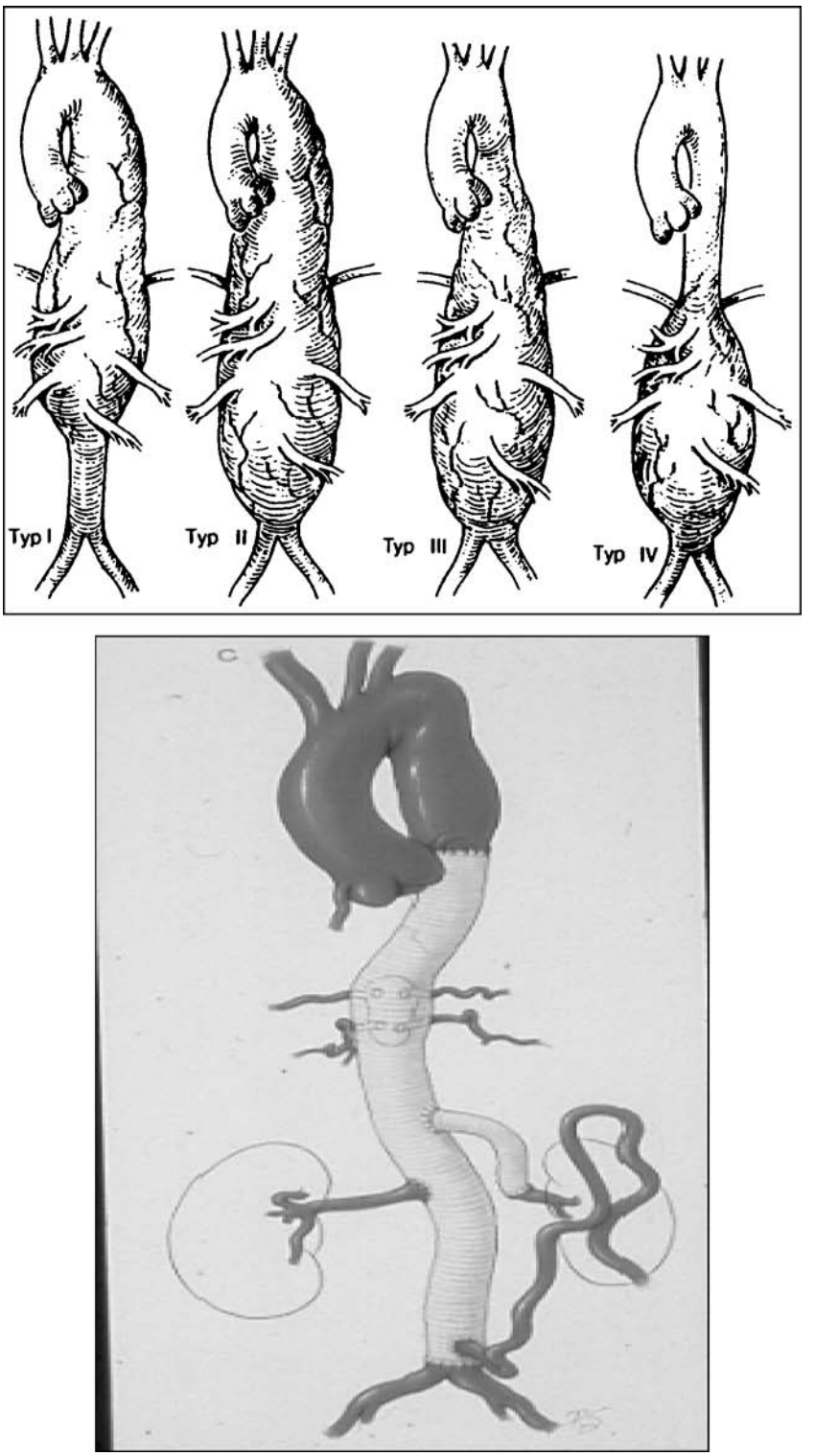

Fig. 3. Schematic demonstration of classification of thoracoabdominal aortic aneurysms (TAA) according to [19] and the surgical interposition of prosthesis. Type I = thoracoabdominal aorta without visceral arteries; Type II = thoracoabdominal aorta with visceral arteries; Type III = distal thoracoabdominal aorta with visceral arteries and infrarenal aorta; Type IV = abdominal aorta with visceral renal arteries

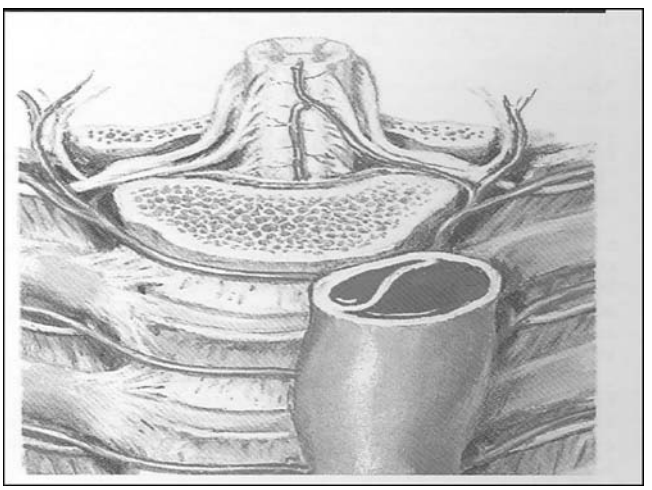

Fig. 4. Abdominal aneurysm with occlusion of A. radicularis magna (Adamkiewicz) resulting in ischemia of the lower spinal cord with an ensuing paraplegia.

Teflon tube (Vygon company, Aachen). The distance between the two metal contacts is 15 mm. The electrode is adequately flexible not to injury neural tissues in the subarachnoid space, and stiff enough to be advanced 3–4 cm in the epidural space so that the tip of the catheter reaches Th4 (Figure 5).

The diameter of the electrode is 0.75 mm and it fits within the hole of a 17-gauge Tuohy needle. The same type of electrode is also used for stimulation purposes. To record a large potential as possible, the recording electrode is introduced into the subarachnoid space utilizing a 17-gauge Tuohy needle after performing a puncture at the lower lumbar level (Figure 6).

Once the tip of the electrode is placed in the epidural space, it can be advanced rostally by gently pushing. As the surface of the spinal cord is covered by the pia mater the flexible tube type electrode does not penetrate into the spinal cord. For routine montage to record SCEP but also the MEP, the tip of the electrode is located at the thoracic

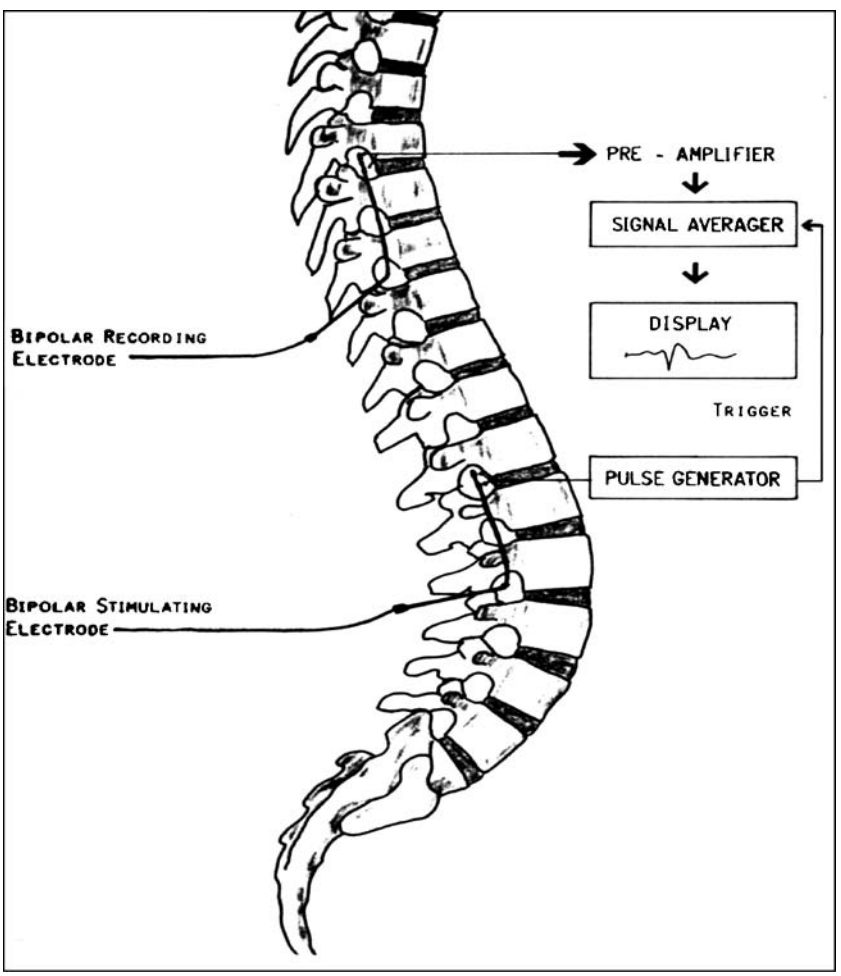

Fig. 5. Schematic drawing in positioning of bipolar stimulation and recording electrode for SCEP monitoring during TAA repair.

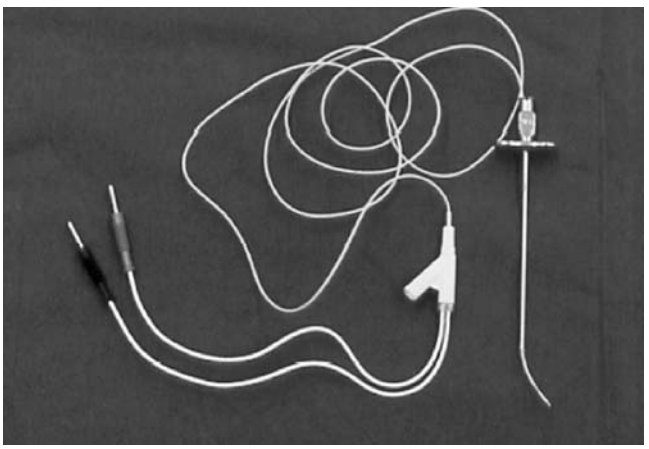

Fig. 6. Bipolar Bipacing-Cath® stimulation and recording catheter (Vygon company, Aachen/Germany). This electrode can be introduced into the intrathecal as well as the epidural space via a 17-gauge Tuohy needle.

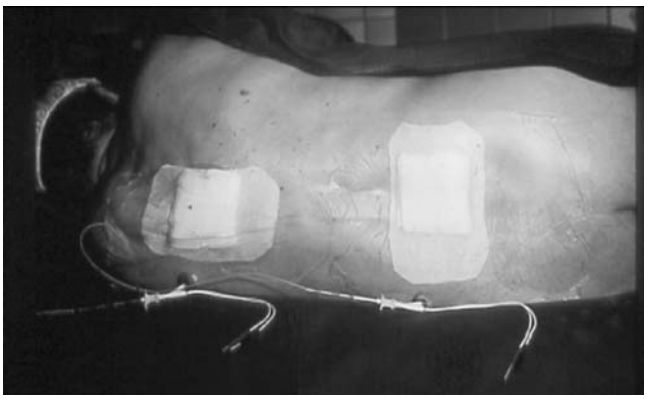

Fig. 7. In situ placement of the two epidural electrodes prior to induction n of anesthesia in a patient undergoing TAA repair.

level or close to the conus medullaris. This peridural placement of the recording electrode allows frequent monitoring with a rapid recognition of the response even in the hostile electrical environment of the operating theatre.

Epidural recording can be performed by inserting a similar type of electrode into the epidural space at the thoracic level. Both electrodes routinely are placed into the epidural space using a percutaneous technique. It is a rule to perform percutaneous epidural puncture prior to anesthesia, when the patient is alert and in the induction area. This is necessary in order to guarantee proper positioning and evoke a sufficient response. Due to mass muscular movement, the intensity of the stimulus necessary to evoke an amplitude of the electrical potential generated in the spinal cord is 1/3–1/2 of that being used in intraoperative recording. Electrode introduction into the epidural space is safe and easy because lumbar puncture is always performed at the level of lower lumbar level and involves no risk to injure the spinal cord, and an anesthesiologist, experienced in thoracic epidural catheter placement, usually performs placement of the electrode at the higher thoracic level. After more than 300 cases that underwent monitoring with this type of electrode insertion, no serious complications have been encountered, except for three cases of malpositioning in which electrode repositioning could not even be corrected by use of fluoroscopy. It should, however be noted that every effort should be made to introduce the electrodes in an absolutely sterile fashion (Figure 7).

This monitoring technique has two advantages over conventional techniques. First, it is possible to eliminate recording of the peripheral posterior tibial nerve, which usually gets ischemic when the aortic is clamped. Thus, only those afferent central nervous system sensory pathways are monitored that are endangered by aortic clamping. Second, the recording catheter records only spinal evoked action potentials. Cortical derived signals, which usually are sensitive to changes in the level of anesthesia and to the considerable temperature changes of the patient, are not recorded. With such a recording technique a useful prognostic indicator for postoperative monitor outcome is at hand which also sets the indication for additional protective measurements. The value of this type of monitoring has been shown in over 300 patients [1] with low, moderate and high risk in developing a neurological deficit could be differentiated according to time till loss of potential and total loss of the SCEP potential being monitored intraoperatively. Especially the time till loss of potential was a sensitive marker to neurological outcome demonstrating a high correlation coefficient of $r^2 = 0.892$ [2]. Whenever early loss was observed this served the surgeon as a guide to reinstall intercostal arteries, thus providing a reperfusion of the spinal cord.

RECORDING OF SPINAL EVOKED POTENTIALS – PRACTICAL ASPECTS

Once the electrodes are placed in appropriate location, it is easy to evaluate the exact stimulation and recording site. Electrical stimulation is delivered to the spinal cord through a 17-gauge bipolar tube type electrode catheter (Bi-pacing-Cath) placed in the epidural space. The electrode, which is on the side of the recording electrode, is used as cathode. The rectangular electrical stimulus is 0.3 msec in duration, 10–13 mA in intensity (1 mA above motor threshold, determined at the awake control period), and 2 Hz in frequency, using a filter setting between 30–3 Hz. To improve signal to noise ratio, 64 signal sweeps are averaged. In cases with normal spinal cord function, averaging is not always

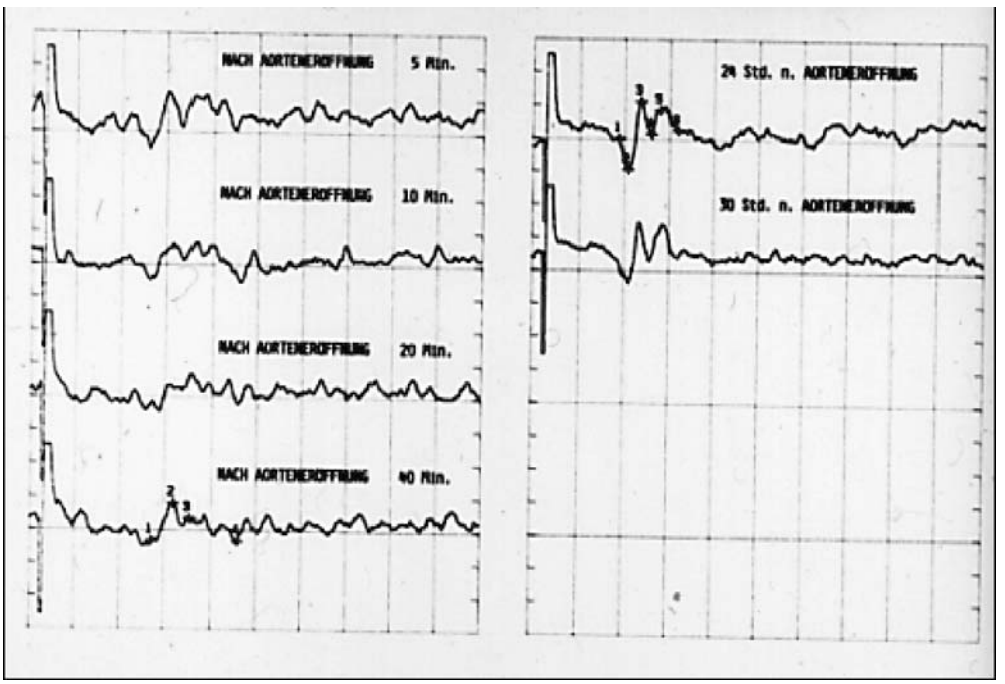

Fig. 8. SCEPs recorded from the peridural space at the level of Th11 after stimulating the spinal cord at L2. SCEPs are characterized by an initial spike wave and a following polyphasic wave component. In the present case SCEP degraded in amplitude after cross clamping. This change is judged as the result of spinal malperfusion. Notice the change after reimplantation of intercostal arteries, which indicates a recovery of spinal cord function.

necessary because the amplitude of SCEP is large enough. In such cases it is possible to perform real time monitoring observing potentials at every 1 second without averaging. It is not possible to describe a standard waveform of the SCEP. The signal configuration differs from patient to patient and is influenced by delicate differences of relation between the stimulating and recording electrodes. Basically, the recorded SCEP consists of an initial spike wave followed by polyphasic waves (Figure 8). Usually the amplitude decrement of the initial spike wave is used as an indicator of spinal cord insult [8]. As spinal cord volleys are highly reproducible in nature, Burke et al. suggested that an amplitude change of 20–30% is a sufficient indication to warn the surgeon [5]. On the other hand, other researchers have suggested that 50% attenuation of the amplitude is the sign of a critical condition in patients with normal spinal cord function [8, 9, 17]. This standard is commonly accepted in SCEP recording [4].

The criterion to regard the spinal cord in critical condition is around 50% decrement of the initial spike wave potential. Attention should be paid to the polyphasic wave portion of the SCEP if intra-spinal cord manipulation is carried out. This part of the potential reflects the dorsal column pathway. A selective insult to the dorsal column, therefore, affects the wave configuration of polyphasic wave of the SCEP. In addition, positioning of the catheter tip can be verified by fluoroscopy. This monitoring technique has two advantages over conventional techniques. First, it is possible to eliminate any recording of the usual ischemic effect of aortic clamping on the peripheral posterior tibial nerve. Thus, one monitors only those afferent central nervous system sensory pathways that are endangered by aortic clamping. Second, the recording catheter records only spinal evoked action potentials. Cortical derived signals usually are sensitive to changes in the level of anesthesia and to the considerable temperature changes of the patient.

Sensory evoked potentials have been advocated as a method to provide insight on any functional deficit of the spinal cord during aortic clamping [20, 21, 23, 25]. From the clinical results one can draw several conclusions. First, sensory evoked potentials recorded during aortic clamping can help predict the postoperative neurologic outcome. Published data show a strong correlation between the recovery time of the evoked potential and the postoperative neurologic outcome in patients [1]. This observation is corroborated by data from an animal study using a similar monitoring set-up [26, 27]. Second, patients who do not loose their evoked potential during aortic clamping show no signs of postoperative motor deficit. In such cases normal sensory nervous pathways, as monitored with the SCEP, were related to normal motor function. Data also indicate that in spite of the known lower ischemic tolerance

of motor compared with sensory nervous pathways [28], the evoked potential can act as a guide of postoperative motor outcome. Other investigators, however, deny any link between the induced sensory evoked potentials and motor function [29]. This difference in opinion may be due to the difference in recording techniques. Monitoring data when derived via direct stimulation of, and recording at, the spinal cord is in contrast to evoked potential monitoring used by other researchers who use stimulation of the posterior tibial nerve. A peripheral nerve, such as the posterior tibial, becomes ischemic during aortic cross clamping. Therefore, one cannot derive definite conclusions on the function of the sensory pathway within the spinal cord when a peripheral nerve is used. Third, following transient ischemia, a close relationship between sensory and motor pathways does seem to exist. This is corroborated by animal studies and by the neurologic outcome in animal and human studies, which show a close correlation with recovery time of the evoked potential after declamping [3, 26, 27]. The time of recovery may represent a useful prognostic indicator for the possible postoperative motor outcome during TAA repair. The SCEP thus can indicate the need for further protection of the spinal cord, such as administration of superoxide dismutase or other oxygen radical scavengers. This is because they may serve as a scavenger of toxic oxygen radicals, which seem to be responsible for the "reperfusion injury" [3, 30–32].

In summary, loss of SCEPs within 15 minutes of aortic cross clamping during TAA repair shows poor collateralization and mandates early restoration of spinal cord blood supply. Additional reattachment is performed at the level of Th8–Th11 to ascertain that a left intercostal artery with slow or minimal back bleeding and a big lumen is the relevant vessel for spinal cord supply. If the SCEP however does not return to normal, then stepwise reimplantation of segmental arteries at the descending aorta and the proximal abdominal aorta is done.

If the surgeon by subsequent separate reimplantation of intercostal arteries can achieve the return of SCEPs to normal, paraplegia will not occur and paraparesis will be rare and mild. Spinal cord monitoring therefore can be regarded as a valuable guide to detect, whether the spinal cord is at risk and to take measures against paraplegia.

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