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ıon clinical applications today

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rology today to confirm and localize sensory abnorm- standardized. Normal limits are now well described. arious types of neurologic disorder. Intensive care unit f these tests. Evoked potentials have become useful as easy to use in many clinical settings. © 1998 Elsevier

ve; Somatosensory evoked potential; Visual evoked

evoked potential abnormalities are called silent st EP peaks are stable, often being of identical ave shape and amplitude in individual patients ted even year to year. The tests are quite objec- they cannot be influenced by the patient's lack on, except for such obvious maneuvers as clos- yes during visual EP testing. EP latencies are to 2–3 significant figures, making them quite scientific study using parametric statistical ana- ore, EPs have been useful in clinical investiga- he pathophysiology of certain neurological

commonly used clinical evoked potentials now kerboard visual EPs (VEPs), the brain-stem (BAEPs), and the median and posterior tibial sensory EPs (SEPs). These are now routinely nost hospitals and many neurological practice are relatively easy to obtain on most patients, EP and SEP tests often are of better quality ent is tested asleep.

ked potentials

scientific and clinical reports on VEPs used testing. Subsequent clinical investigations

described the superiority of checkerboard VEP techniques. The latter more readily identified optic neuritis by taking advantage of the visual system's preference for edges, contrast and movement perception. The commonly used clinical checkerboard technique employs a screen displaying 30 arc-minute black and white squares arranged in a checkerboard pattern with checkerboard reversals timed to occur twice per second. The techniques produce a large, easily distinguished occipital positive potential at about 100 ms after each checkerboard reversal. These are most easily recorded 5 cm above the inion in the midsagittal plane.

The principal clinical changes observed are delay in latency and reduction in amplitude of this primary occipital 100 ms positive potential, named the P100. Latency delays of 10–30 ms or more commonly occur in optic neuritis. Ischemic and compressive diseases of the eye and optic nerve produce diminished amplitude of the VEP with little or no latency delay. A variety of neurodegenerative conditions and other disorders can produce bilateral latency delay, often of a mild degree. One can sometimes distinguish the type of pathology underlying a VEP abnormality by making use of these general rules. For example, a unilateral 30 ms latency delay without loss of amplitude, with normal results in the other eye, almost always is the result of an optic neuritis in the affected pathway. The general rules about latency and amplitude changes are summarized in Table 1.

The demyelinating type of change, characterized by asymmetric latency delays or severe latency delays, are typical of multiple sclerosis (MS) with optic neuritis. They are uncommon in any other setting. The VEP is abnormal in 90% of patients with definite MS and 70% of patients with probable MS. The VEP is also abnormal in 55% of those MS patients who have no signs or symptoms of visual pathway problems. In this latter group, identification of a silent lesion by VEP abnormalities can provide evidence of a second or third lesion, thereby helping to establish the diagnosis of MS.

The compressive type of VEP change, a unilateral amplitude loss, with possible mild latency change, is seen in compression of the optic nerve, ischemic optic neuropathy, amblyopia and glaucoma. In these conditions, VEP may show changes even when vision is still otherwise quite normal.

The degenerative type of VEP change, with mild to moderate symmetric latency increase and possible mild symmetric amplitude loss, is seen with a variety of specific conditions. This includes some of the spinocerebellar diseases, and some other specific neurodegenerative conditions, such as B_{12} deficiency, and may also been seen in multiple sclerosis if bilaterally symmetric optic neuritis is present.

For an extended review of EPs in MS, see Nuwer (1996). Good extended reviews of VEP techniques and applications include those of Chiappa (1993) and Celesia (1992).

Other types of VEPs are sometimes used clinically. In children, checkerboard testing can be difficult. Flash VEPs are sometimes used in those patients. Flash can be done with a traditional strobe, or occasionally with light-emitting diodes placed into goggles, which are strapped to the patient's face. Occasionally, half-field VEPs are used to help assess evidence of retrochiasmatic lesions.

3. Brain-stem auditory evoked potentials

BAEPs have become widely used to assess the clinical state of the middle portion of the brain-stem as well as for assessment of hearing. It is often applied for screening hearing in infants who are at high risk for hearing loss.

BAEPs test acoustic conduction through the ear, the eighth cranial nerve, into the lower pons, and continuing rostrally in the lateral lemniscus up the brain-stem. A series of 5 or more peaks are recorded from the scalp vertex. BAEPs can be recorded easily in patients who are comatose or sedated, advancing their usefulness in the intensive care unit (ICU).

BAEPs are produced by a brief square wave electrical pulse to earphones, usually using a 100 μs pulse. These clicks are presented at 10–70 times per second. At fast rates, data can be collected more quickly, but the peaks become less well defined. Stimuli are often delivered at about 70 dB HL intensity. Somewhat higher in patients with pre-existing hearing impairment. For testing of hearing itself, a variety of separate intensities are often presented. Recordings are made from the scalp vertex, with reference electrode at the ear ipsilateral to stimulation. A second channel is often used with recording from the scalp vertex to the contralateral ear. A series of 5 or more brief peaks is seen in the 6–8 ms after each click presentation. Since these peaks are less than 1 μV in amplitude, the clicks must be presented several thousand times to average out all background activity. The classical BAEP peaks are labeled with Roman numerals I-V. The several succeeding peaks VI-VIII are quite variable, and are therefore not generally clinically used. Standards for testing are set forth by publications such as Nuwer et al. (1994b) and American EEG Society (1994). Examples of typical peaks are shown in Fig. 1.

Wave I is generated from the portion of the eighth cranial

Table 1
Types of VEP changes

Type of abnormality	Latency delay	Amplitude loss	Asymmetry of changes
Demyelinating	++	±	+
Compressive	±	++	+
Degenerative	+	±	-

Three types of VEP changes are shown, contrasting the finding among the types: -, not seen; ±, none or mild degree occurs; +, present; ++, prominent feature.

including demyelination, ischemia, tumors, ve disorders or with severe posthypoxic brain- ürment. The typical upper limit of normal for erpeak interval is 4.5 ms. For full-term neonates, erpeak interval should be less than 5.4 ms.

I interpeak interval assesses conduction from the eighth nerve into the contralateral lower pons. vay can be impaired by tumors at the cerebello- gle, inflammation in the subarachnoid space, or ders affecting the pontomedullary junction where nerve enters the brain-stem. It can also be dis- he pathway crosses through the lower pons, such al pontine myelinolysis. Usually, delays of I-III interval are not considered clinically significant re is an accompanying prolongation of the I-V interval.

-V interpeak interval reflects conduction from s to upper pons or lower midbrain. There is not te agreement about the side on which the wave V nerated, although the preponderance of evidence te contralateral to the stimulated ear. This portion iway is affected by intrinsic brain-stem disorders myelination or tumors.

e amplitudes of BAEP peaks vary widely among bjects. To reduce this intersubject variability, the nplitudes is calculated for waves V and I. Using one can assess whether wave V is relatively small ison to wave I. A small wave V implies an intrin- tem impairment, whereas a small wave I implies a earing impairment.

sence of waves I, III, and V is also assessed when ıg whether a BAEP is normal. Wave II is an vave, i.e. not present in some normal subjects. ometimes blends or merges into a IV-V complex, onsidered to be a normal variant. For a BAEP to , waves I, III and V should be present and well ith normal interpeak intervals and V/I amplitude

neasuring hearing, the BAEP is also tested at low Low stimulus intensity reduces the peak ampli- causes a prolongation of peak latencies. The peak hange in a systematic way that can be tracked and Decreases in intensity even further leads to an f all waves. This point at which the BAEP disap- eferred to as the threshold. The threshold for approximately the same as it would be for tradi- iometry testing in the frequency range of 500–

AEP is abnormal in greater than 95% of patients an acoustic neuroma or other cerebellopontine ors. It is also abnormal in a high rate of patients brain-stem glioma, or other focal brain-stem ıt at a midpontine level. Central pontine myelino- rain death both cause disruption of function at a vel. Hearing loss produces changes in the BAEP and in the latency-intensity curve.

BAEP is abnormal in about 70% of patients who have a subarachnoid inflammation from subarachnoid hemorrhage, meningitis or Guillain-Barre syndrome. In these circumstances, the abnormality is primarily an increase in the I-V and I-III interpeak intervals. BAEP is also abnormal in about 70% of patients who have multiple sclerosis with signs of symptoms of brain-stem impairment.

BAEP is abnormal in about 40% of patients who have MS without signs or symptoms of brain-stem impairment. These signs and symptoms most frequently associated with BAEP abnormalities are those of internuclear ophthalmoplegia and related eye movement signs in MS. Some CNS degenerative disorders also affect BAEP latencies or V/I amplitude ratio. In a general manner, neurodegenerative disorders affecting the brain-stem produce BAEP abnormalities in about 40% of patients in these various diagnostic categories. Good general reviews of BAEPs include those of Chiappa (1993), Picton et al. (1992) and Stockard et al. (1992).

4. Somatosensory evoked potentials

Median nerve SEP begins with transcutaneous delivery of an electrical stimulus to that nerve at the wrist. A 100–300 μs square wave electrical pulse is delivered at intensities strong enough to cause a 1–2 cm thumb twitch. Upon delivery of such a stimulus, nerve action volleys travel orthodromically up sensory fibers and antidromically up motor fibers to the shoulder, producing a peak as they enter, and traverse the brachial plexus region. This brachial plexus peak is best detected at a point on the shoulder called Erb's point above the proximal clavicle. The peak itself is often referred to as the Erb's point peak, although more formally it known as N9. In the course of conduction, the sensory fibers then transverse the cervical roots and enter the cervical cord. The median nerve pathway then joins the posterior columns, sending off collateral branches to synapse in the midcervical cord. This midcervical cord activity gives rise to a peak known as N13. The N13 is best measured from skin over the fifth cervical spine. Further conduction rostrally in the posterior columns passes through the synapse at cervicomedullary junction and enters the lemniscal decussation. A scalp positive P14 peak is detectable which is generated from the pathway at this level. As conduction continues up the medial lemniscus to upper midbrain and into the thalamus, a scalp negative peak is detected, the N18. After synapsing in thalamus and traversing internal capsule, the N20 is recorded over somatosensory cortex contralateral to the wrist stimulated, corresponding to arrival of the nerve impulses at its primary somatosensory region. Technical standards for SEPs are set forth by publications such as Nuwer et al. (1994a) and American EEG Society (1994). An example of median nerve SEPs is shown in Fig. 2.

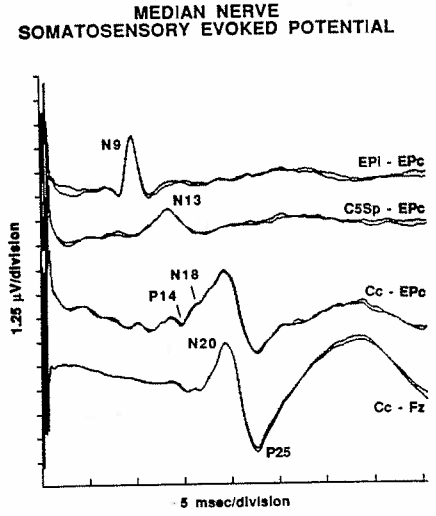

Fig. 2. SEPs from median nerve stimulation. Typical peaks are shown in each of the 4 recording channels. The test results are normal. Negative polarity at the first electrode cited is shown as upward deflections. Recording sites EPi and EPc are at the ipsilateral and contralateral Erb's points on the shoulder; C5Sp is over the fifth cervical spine; Cc is 2 cm posterior to C3 or C4 contralateral to the side stimulated; Fz is at its standard 10–20 system site. From Nuwer et al. (1994a).

Posterior tibial nerve stimulation at the ankle gives rise to a similar series of subsequent peaks. An N8 potential can be detected over the posterior tibial nerve at the knee. An N22 potential can be detected over the upper lumbar spine, corresponding to the collateral activity as the sensory fibers synapse in the lumbar spinal cord. More rostrally, a cervical potential can occasionally be detected over the mid- or upper cervical spine, although this may not be seen in many normal subjects. Finally, a P37 scalp positive potential is seen over the midline scalp lateral to the midsagittal plane, but ipsilateral to the leg stimulated. This is a paradoxical localization in that the scalp positive potential appears on the scalp contralateral to the hemisphere generating it. This occurs in part because the region generating the P37 potential is deep in the interhemispheric fissure, with a dipole pointing across the midsagittal plane. An example of posterior tibial nerve SEPs is shown in Fig. 3.

Median and posterior tibial SEPs are used in a variety of clinical settings. They can detect, localize and quantify focal interruption along these pathways. Such disruption may be due to any number of focal neurological problems, including trauma, compression, multiple sclerosis, tumor or other focal lesions.

SEPs also detect diffuse slowing and cortical attenuation from diffuse CNS disorders. This is seen in a variety of neurodegenerative disorders, and metabolic problems such as B_{12} deficiency. When a patient suffers from sensory impairment, and when the clinical localization of the sensory impairment is unclear, SEPs can be helpful by distin-

ionally, SEPs can be helpful in patients with per-
nervous system impairment. For example, some
suffer from substantial degrees of peripheral
ent so that nerve conduction velocity testing can-
irectly performed. In some patients, indirect mea-
ts of nerve conduction velocity can be done using
niques. For example, one can stimulate at the wrist
sure cortical potentials, and then subsequently sti-
t the elbow and record cortical potentials. By sub-
latencies and distance, one can get an indirect
nent of nerve conduction velocity from wrist to
Good general reviews of SEPs include those of
t al. (1993), Chiappa (1993) and Aminoff and
992).

d potentials in the ICU

eral, ICU use of EPs includes the BAEP and SEP.
ve been found to be much less useful in the ICU
BAEP and SEP can help to assess prognosis for
patients (Chatrian et al., 1996; Chen et al.,
sch Blancafort et al., 1995; Krieger et al., 1995).
's, the prognostic error rate can be cut in half com-
monitoring just with the Glasgow Coma Scale,
ial pressure monitoring, neuroimaging and other
nformation. In barbiturate coma and drug over-
Ps can help to separate drug effects from true
nage. This can be done because barbiturates and
zepines have little effect on short latency EPs, even
doses sufficient to produce an isoelectric EEG.
n death, EPs are not necessary in routine cases.
their use is encouraged for cases in which the
th determination is difficult, open to dispute, or
the usual physical examinations or tests are hard
ard to interpret (Wijdicks, 1995).
red to the physical examination, the BAEP is use-
ally if the eyes or face cannot be examined prop-
mpletely. The absence of a wave I in a BAEP
robable damage to the peripheral portion of this
In coma, this may occur because of traumatic
coma that also disrupt the auditory pathway, or
lly may occur because increased intracranial pres-
s ischemia in the territory of the vestibular artery.
e of an absent wave I in a BAEP, the clinician is
aware not to trust the absence of a doll's or a
st, since the sensory end organ may be non-func-

waves III-V are absent in patients comatose after a
rest, essentially all of the patients go on to die or
getative outcome. After head trauma, the absence
III-V is also associated with very poor neurologic

nts who are comatose after a cardiac arrest, wave
cy increases are generally proportional to the
of the outcome. Patients with a more severely

abnormal I-V BAEP often have the worst prognosis in this patient group. In head trauma, increases in I-V interpeak interval are somewhat less successful at prognosis.

Patients in coma after arrest or head injury, or after CNS infection, who also have a normal BAEP generally have a good survival (80–100%) and many of these have good neurologic outcomes.

The somatosensory median nerve evoked potential is helpful in coma. If the cortical peaks N20 and subsequent peaks are completely absent 24 h or more after a cardiac arrest, essentially all of the patients go on to die or have vegetative neurologic sequelae. Conversely, in a patient deeply comatose after cardiac arrest, the finding of normal cortical N20 and subsequent waves imply that the patient has a good prognosis for eventual neurologic recovery, and that the medical team should continue to work hard to support the patient in the interval. Good general reviews of EPs in the ICU are found in Chiappa (1993), Nuwer (1994) and Chatrian et al. (1996).

6. Evoked potentials in surgery

Evoked potentials have been very successful in providing a means for monitoring and testing in the operating room (OR). Both BAEP and SEPs have been used in OR testing as well as in monitoring. Testing with median nerve SEPs has been useful to identify the sensory and motor cortex during craniotomies. By seeing the N20 peak and localizing its dipole, the neurophysiologist can identify the postcentral cortex subserving sensory function. With this known, one can readily deduce the location of motor cortex. Techniques used resemble those for routine EP testing, except for the use of special electrodes designed for recording directly from exposed cortex. In some cases, multichannel recording from a strip or grid of electrodes can speedup the identification.

Monitoring with SEPs has been useful for spinal cord and brain-stem surgery. Monitoring BAEPs has been useful in posterior fossa surgery. The goal of monitoring is to identify acutely impaired function along these pathways, alerting the surgeon to the impending complications. Quick action can reduce or eliminate the causes of such complications. In this way, monitoring can substantially reduce the risk of postoperative neurologic sequelae.

Posterior tibial nerve SEP monitoring has been used widely for monitoring the spinal cord during scoliosis procedures and other surgical interventions in which the spinal cord is at risk for damage. The techniques resemble those used in ordinary outpatient SEP testing. The anesthesiologist needs to avoid certain inhalation anesthetic agents which can abolish the cortical SEP. Recording of far field intracranially generated peaks can help to allow monitoring even when the primary cortical peaks are impaired due to anesthetic agents. At some centers, epidural electrodes are used around the spinal cord itself, giving a more direct measurement of spinal cord function during such surgery. Evoked potential spinal cord monitoring can reduce by one-half the rate of serious spinal cord damage during surgery around the spinal cord (Nuwer et al., 1995).

Median nerve SEPs have been used in monitoring surgery at the midcervical or upper cervical levels. Both median nerve SEPs and BAEPs have been useful for surgery in the posterior fossa. At that site, BAEPs can also monitor eighth nerve function as well as integrity of brain-stem pathways. Such monitoring has identified ways in which surgeons impair the brain-stem through retraction, leading to changes in surgical techniques. In many cases, these monitoring techniques allow the surgeon to proceed, knowing that these pathways remain intact.

Occasionally, the median nerve SEPs are used to monitor during cross-clamping of the carotid artery. This technique can be used instead of EEG or together with EEG monitoring in such cases. EEG has the advantage that it monitors many separate regions of the brain, whereas median nerve SEP only measures certain specific pathways leading to the postcentral cortex.

Over time, EP testing and monitoring in surgery have become standard techniques widely used and well accepted to enhance surgical techniques and reduce risk of postoperative neurologic problems for the patient. Good general reviews of these techniques and their applications can be found in Nuwer (1986), Nuwer et al. (1993), Møller (1995) and Russell and Rodichok (1995).

7. Summary

In many ways, evoked potentials have become standard tools used in the care of certain patients with neurological problems, including patients cared for in the ICU and in some surgical procedures. The techniques have found acceptance because they are relatively objective, reproducible, very sensitive to impairment, and relatively easy to use in many clinical settings. The ways in which evoked potentials can be used continue to grow and evolve. Even at the present, techniques for carrying out routine clinical pyramidal pathway motor evoked responses are being evaluated, and these will certainly soon come into widespread use as well.

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Evaluation and prognostication in coma

Keith H. Chiappa*, Rosamund A. Hill

Massachusetts General Hospital, EEG Laboratory, Boston, MA 02114, USA

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Abstract

Electroencephalography (EEG) and evoked potential (EP) studies are neurophysiologic techniques which provide information on physiological state and response to therapy, and may aid diagnosis and prognosis. Serial studies or continuous monitoring may enable changes to be detected prior to irreversible deterioration in the patient's condition. Current computer technology allows simultaneous display and correlation of electrophysiologic parameters, cardiovascular state and ICP. Continuous EEG monitoring in the ICU has been shown to have a decisive or contributing impact on medical decision making in more than three-quarters of patients. In addition, continuous EEG monitoring has revealed previously unsuspected non-convulsive seizures in two-thirds of patients. Somatosensory and auditory EPs can provide useful prognostic information in coma patients, however, these tests are etiologically non-specific and must be carefully integrated into the clinical situation. Motor EPs offer a potentially useful tool for evaluating motor system abnormalities in the ICU. Thus, neurophysiologic tests are established monitoring tools in the neurological intensive care unit. © 1998 Elsevier Science Ireland Ltd.

Keywords: Coma; Diagnosis; EEG; Intensive care unit; Prognosis

1. Introduction

Neurophysiologic techniques (electroencephalogram and evoked potentials) are used in the neurologic intensive care unit (neuro-ICU) for: (1) monitoring physiological state, (2) response to therapy, (3) supplementing or replacing the neurological examination in coma and/or paralysis, iatrogenic or natural, (4) prognosticating, and (5) defining the disease process. In addition, the computer technology that manages the large volume of data generated by electrophysiologic monitoring is useful for the analysis and display of other data collected in the neuro-ICU. Combined computer displays show trends in the EEG, evoked potentials, intracranial pressure, blood pressure, heart rate, and others, and it is only these combined displays which allow effective study of the interaction between these variables.

2. Assessing CNS function in the ICU

Serial neurologic examination is not an adequate way to monitor central nervous system (CNS) levels of functioning in the neuro-ICU. Patients may be therapeutically paralyzed and serial neurologic examinations, even when performed conscientiously, are discontinuous, may miss important changes in the patient's condition and vary according to the expertise of the examiner. A single or even repeated electrophysiologic study may suffer from the same problems: it is a discrete, brief sample of data that may not reflect the patient's overall condition. However, the electrophysiologic studies may yield brain wave patterns (e.g. suppression, burst-suppression, spindles, seizures, cycling) or evoked potentials which have possible therapeutic and prognostic significance.

Advances in technology have made possible the collection, storage and analysis of continuously collected EEG and repeated evoked potentials. Extensive standards for electrophysiologic monitoring have recently been published (Chatrian et al., 1996). Such monitoring should enable the clinician to detect CNS injury at a time when meaningful intervention is still possible. For example, when temporal lobe herniation has reached the stage of third cranial nerve compression and pupillary dilation, a common signpost, some irreparable damage has probably already been done. In the case of arterial occlusion or vasospasm, clinical signs may be instantaneous or hours can intervene between the occlusion and clinical manifestations. In these cases, the EEG would change dramatically and could be used as a

* Corresponding author. Tel.: +1 617 7268737; fax: +1 617 7262019.

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