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Basics of Evoked Potentials

Evoked potentials are electrical potentials recorded over various parts of the nervous system in response to sensory or motor stimulation. Each stimulation results in a low amplitude evoked response. In order to adequately visualize and measure these responses, evoked potentials are usually averaged and amplified. When many *evoked responses* have been averaged, they are referred to as an *evoked potential*. Each evoked potential has a series of waves or peaks in response to the stimulus.

Types of Evoked Potentials

Clinical evoked potentials performed in a clinical laboratory most often involve stimulation of one of the sensory systems and recording the evoked potentials off peripheral nerves, spinal cord, or brain. The motor pathways can also be stimulated with an electrical or magnetic stimulus; however, neither of these is done routinely in an outpatient environment. Electrical stimulation is too painful in an awake patient, and magnetic stimulation is mostly used in research applications. Evoked potentials are named according to the neural pathway that is stimulated.

Modalities

Three types of evoked potentials are routinely used in clinical practice: visual, auditory, and somatosensory. Visual evoked potentials (VEPs) are obtained with light flashes or a patterned stimulus like a checkerboard. These are called flash VEP (FVEP) and pattern reversal VEP (PRVEP), respectively. Auditory evoked potentials (AEPs) are obtained with an auditory stimulus, most often a broadband click. Somatosensory evoked potentials (SEPs) are obtained with electrical stimulation of peripheral nerves. Most often large mixed nerves are stimulated to obtain SEP. In the upper extremity, median and ulnar nerves are used most often, and in the lower extremities tibial and peroneal nerves are used.

Each type of evoked potential consists of several peaks occurring at latencies ranging from a few ms to several hundred ms after stimulation. Peaks are designated as short, middle, or long latency waveforms depending on when they occur. In general, short latency waveforms are clinically more useful as they are more easily reproducible, consistently identified in normal subjects, and resistant to medication effects. Short latency AEPs occur within 10 ms after stimulation and are called brainstem auditory evoked potentials (BAEPs). Short latency SEP occur up to 30 to 50 ms after stimulation and are used clinically. VEP responses are long latency potentials that occur at about 100 ms.

Nomenclature

The individual peaks of the evoked potentials that are important in clinical evaluation are named according to their latency after stimulation, polarity, or number in a sequence. VEP and SEP peaks are named based on their polarity and typical latency in a normal adult. Thus, the P100 waveform of the VEP is a positive potential that typically occurs at a latency of 100 ms. The N34 waveform of the tibial nerve SEP is a negative peak that typically occurs at a latency of 34 ms. BAEP peaks are

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named according to the order in which they appear; consequently the five BAEP peaks are called waves I–V. Though there is agreement about waveform nomenclature, there is no universal standard on how waveforms should be displayed. Whereas for most neurophysiologic studies negative potentials are displayed with an upward deflection, this is not always true for evoked potentials. Negativity may be displayed as an upward or downward deflection. Regardless of how it is displayed, it should be clearly noted on the study.

Certain peaks are designated as "obligate waveforms." Obligate waveforms are so named because their absence usually denotes an abnormality. Not all waveforms of an evoked potential are considered obligate. In tibial nerve SEP, the lumbar potential (LP) waveform is not considered obligate, so its absence is not necessarily considered abnormal.

Waveform Generators

Evoked potentials are generated when impulses travel through the nervous system. The various components of an evoked potential are generated when there is synaptic transmission or when an impulse is traversing a fiber tract, particularly when that fiber tract changes direction (1). An example of the latter is when a somatosensory impulse ascends from the dorsal horn to the dorsal column pathway. In the cervical region, this transition contributes to the N13 waveform potential seen after median nerve stimulation.

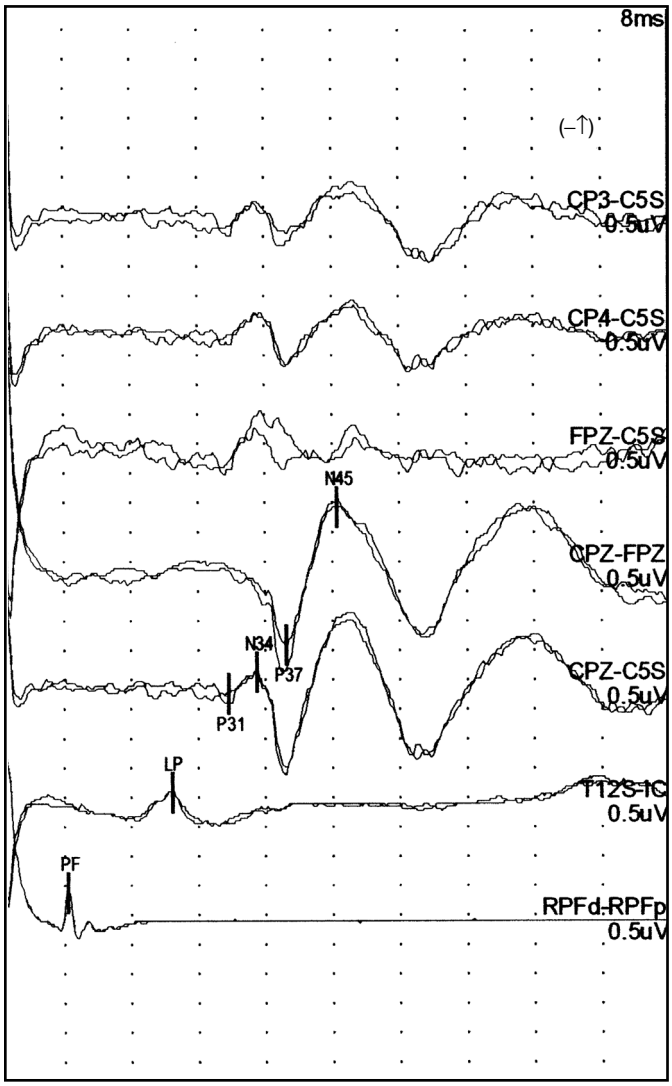
When evoked potentials are recorded close to the generator site, they are referred to as near-field potentials. To record a near-field potential, the recording electrode is placed directly over or very close to the peripheral nerve, spinal cord, or brain structure contributing to the evoked potential. These potentials are often triphasic, with a large negativity preceded and followed by a smaller positivity. The initial positivity occurs due to a wave of depolarization approaching the recording electrode. The large negativity occurs when the depolarization passes beneath the recording electrode, and the final, small positivity occurs due to repolarization. Near-field potentials are of high amplitude and very sensitive to electrode placement. Slight changes in the location of the recording electrode can drastically change the amplitude of the response. The P37 waveform obtained after tibial nerve stimulation is an example of a near-field potential whose amplitude is greatly dependent on the location of the recording electrode (Figure 1.1).

In contradistinction to near-field potentials are far-field potentials. Far-field potentials are recorded from an electrode that is distant to the site of the waveform generator. These potentials are biphasic, with the recording electrode seeing only a moving phase of depolarization through neural pathways. Far-field potentials are of low amplitude and do not significantly change in amplitude and morphology with slight movement of the recording electrodes. The N34 waveform obtained after tibial nerve stimulation is such a waveform (Figure 1.1). Most of the BAEP waveforms (waves II–V) are also far-field potentials. BAEP and SEP contain both near- and far-field potentials. VEP, on the other hand, consist of only near-field potentials.

Evoked potentials can also be thought of as being cortical, subcortical/spinal cord, and peripheral nerve evoked potentials. Cortical evoked potentials are generated by synaptic activity in cortical neurons and the thalamocortical projections. These potentials are usually near-field potentials. The VEP and the later components of the SEP are cortical evoked potentials. Subcortical/spinal cord evoked potentials are produced by impulses moving through fiber tracts and brainstem nuclei. Evoked potentials recorded from brainstem structures are far-field potentials as the recording electrodes are distant to the site of potential generation. Most of the BAEP waveforms are subcortical, far-field potentials. Spinal cord evoked potentials are recorded much closer to their site of generation and are considered near-field potentials. The N13 waveform is a spinal cord evoked potential. Peripheral nerve evoked potentials are recorded from electrodes directly overlying these nerves and represent a wave of depolarization traveling through that nerve. These near-field potentials are often of high amplitude, such as the Erb's point (EP) waveform potential. Peripheral nerve evoked potentials are comparable to mixed nerve action potentials recorded in an electromyography laboratory. Anesthetic medications affect peripheral nerve evoked potentials the least and cortical evoked potentials the most.

Specific neural structures are often regarded as the generators of particular evoked potential waveforms. These associations have been made mostly from lesion and autopsy studies. Waveforms have progressively ascending neural structures assigned to them. When a particular waveform is absent or

Age: 14 years
Sex: Female
Stimulation rate: 5.7/s
Filters: 30–3,000 Hz
Scale: Amplitude = 0.5 µV/div; Latency = 8 ms/div
Side: Right
Stimulation duration: 0.2 ms
Stimulation intensity: 18.8 mA
Number of repetitions: 2,000
Tibial nerve conduction velocity (tibial nerve to T12S): 48 m/s



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
PF	8.30	
LP	20.8	
P31	27.5	
N34	30.8	
P37	34.4	2.38 (P37–N45)

Interpeak Latencies	
Waveforms	**Latency (ms)**
PF–P37	26.1
LP–P37	13.6

Discussion: The P37 waveform is a near-field potential whose amplitude is greatly dependent on the location of the active recording electrode. Notice that the P37 waveform is of high amplitude in the CPz–C5S derivation, but moving the electrode to CP3, CP4, and FPz (top three channels) results in a dramatic change in the amplitude of this near-field potential. On the other hand, the N34 waveform is a low-amplitude, far-field potential. It is clearly visualized in the CPz–C5S derivation, and its amplitude and morphology do not change with moving the active electrode to CP3, CP4, and FPz.

SEP, somatosensory evoked potential.

Figure 1.1 Tibial nerve SEP near-field and far-field potentials.

prolonged, the site of pathology is at or distal to its generator. While clinically useful, this approach is too simplistic and has some shortcomings. First, while particular neural generators are thought to result in certain evoked potential waveforms, it should be recognized that a single nucleus or fiber tract may contribute to more than one waveform. Each waveform in turn may be composed of potentials from many different sites (2). Additionally, evoked potentials do not ascend in the nervous system like an electrical signal through a cable, and evoked potential peaks do not simply represent different points on this cable. Evoked potentials may ascend through several different pathways and since many different components contribute to each waveform, the waveforms may appear out of order. An example of this is sometimes seen with median nerve SEP. Usually the N13 waveform (thought to be generated in the cervical spinal cord) is seen at a shorter latency than the P14 waveform (thought to arise from the nucleus cuneatus). Sometimes, however, the P14 waveform has a shorter latency than the N13 waveform (Figure 1.2). This would be impossible if evoked potential waveforms were simply waypoints in an ascending pathway. In the author's laboratory, the P13 waveform is tagged instead of the P14 waveform; the P13 waveform, the positive waveform immediately preceding the P14, is often better visualized and thought to have the same generator.

Stimulation Methodology

The type of stimulus used to obtain evoked potentials depends on the type of evoked potential being performed. A light flash or patterned stimulus is used for VEP, auditory clicks are used for BAEP, and electrical stimuli are used for SEP. Specific details of each stimulation type will be discussed in later chapters, and here a summary of basic principles is presented.

Electrodes

Stimulating electrodes are used for SEP. BAEP stimulation involves headphones (or ear inserts) while VEP are obtained with visual stimulation. Though both surface and needle electrodes can be used to deliver the electrical stimulus for SEP, surface electrodes are used most often in routine practice. Details of electrode properties are discussed in the following sections.

Parameters

Stimulation parameters include intensity, duration, rate, and repetitions. Varying these parameters may result in alteration of the evoked potential waveform morphology and latency.

Intensity

The lowest stimulation intensity that is needed to produce an evoked potential is known as the threshold intensity. As the intensity increases the latency decreases and amplitude increases. The latency and amplitude change is not linearly related to the stimulation intensity, and the changes occur up to a maximum. Beyond this limit, further increase in stimulation intensity does not affect the evoked potentials. Central components of the evoked potentials reach maximum amplitude earlier than peripheral components. This occurs because of "central amplification" of the stimulus (3). Central amplification refers to the ability of a peripheral stimulus to activate more fibers in central pathways than in peripheral nerves. Consequently, with gradually increasing stimulus intensity, cortical and subcortical evoked potentials will cease to become larger at a lower intensity than peripheral evoked potential. This is discussed in more detail in Chapter 4.

Intensity of stimulation is measured differently for different types of evoked potentials. For SEPs, the intensity is milliampere (mA) of electrical stimulation. BAEP stimulation intensity is measured by the decibel (dB) of the auditory clicks. Intensity of stimulation of PRVEP depends on the contrast ratio between the light and dark patterns.

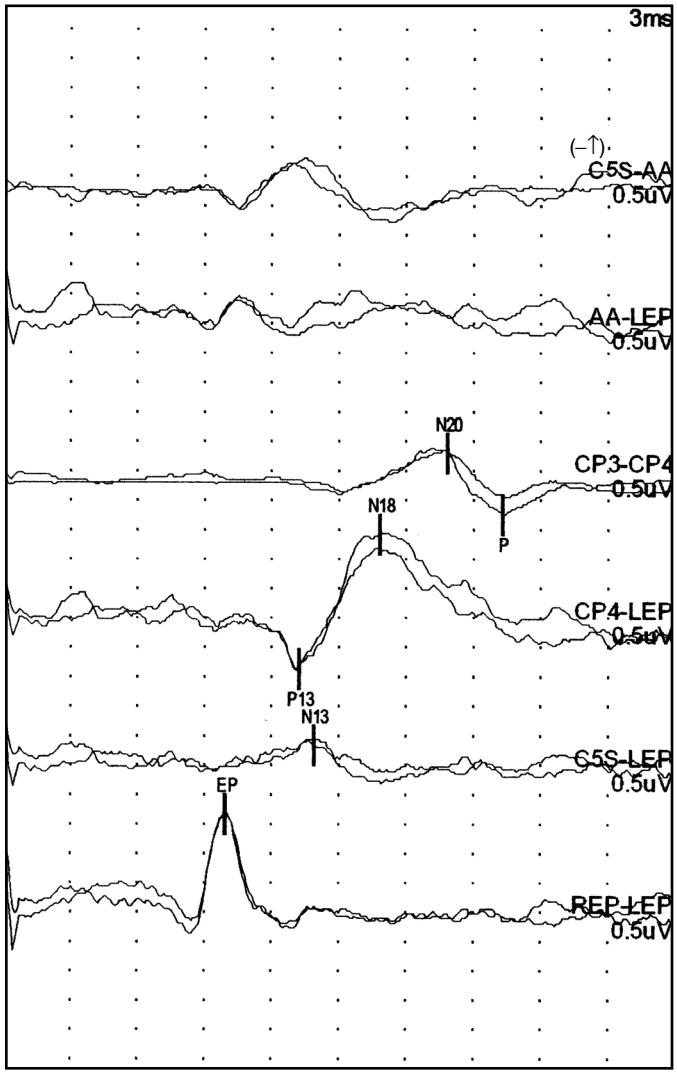
Duration

Duration of the stimulus is closely related to the intensity. It refers to the time that the stimulus is applied. Increasing the duration of the stimulus has an effect similar to increasing intensity. Longer duration stimuli will result in shorter latency and higher amplitude of the evoked potential waveforms with the same caveats as noted above for intensity.

Rate

The stimulus rate is the number of stimuli delivered per second. It is often denoted in hertz (Hz), but this is incorrect, as Hz implies that the stimulus is sinusoidal. The stimulus rate must be such that the entire evoked potential waveform of interest is recorded before the next stimulus is delivered.

Age: 56 years
Sex: Female
Stimulation rate: 5.7/s
Filters: 30–1,500 Hz
Scale: Amplitude = 0.5 µV/div; Latency = 3 ms/div
Side: Right
Stimulation duration: 0.2 ms
Stimulation intensity: 16.4 mA
Number of repetitions: 1,213
Median nerve conduction velocity (median nerve to EP waveform): 46 m/s



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
EP	9.90	
N13	13.9	
P13	13.2	
N18	16.8	2.31 (P13–N18)
N20	19.8	1.08 (N20–P22)

Interpeak Latencies	
Waveforms	**Latency (ms)**
EP–N20	9.90
EP–P13	3.30
P13–N20	6.60

Discussion: The N13 waveform is thought to arise from the cervical spinal cord and the P13 (and P14) waveform from the nucleus cuneatus. In this example, the P13 waveform has a shorter latency than the N13 waveform even though its generator is rostral to the generator of the N13 waveform. This suggests that individual waveforms cannot be considered to arise from single generators. In reality, each waveform receives contributions from several generators and each generator contributes to multiple waveforms.

SEP, somatosensory evoked potential.

Figure 1.2 Median nerve SEP waveform latency variations.

Thus, the rate is dependent on the latency of the evoked potential waveforms. Short latency waveforms require a shorter time window of recording and can be acquired using faster stimulation rates. Long latency potentials require a longer time window of recording and need a slower stimulation rate. For BAEP waveforms, a recording time (or sweep) of 10 to 15 ms can be used with a stimulation rate of 50/s. On the other hand, VEP waveforms often require a sweep of 200 ms, and so must be obtained with a slow rate of about 1 to 2/s. If the stimulation rate is too fast, the evoked potential from one stimulus starts before the evoked potential from the previous one has been completed. This results in steady state evoked potentials. Steady state evoked potentials are not routinely used clinically. The stimulation rate should not be an integer of 60, as alternating current (AC) in power lines in the United States is generated at 60 Hz (it is 50 Hz in some parts of the world). If the stimulation rate is an integer of 60, differential amplifiers may be unable to eliminate the electrical artifact from the evoked potentials recording.

In general, with slower rates of stimulation, the evoked potential waveform morphology is better, latency shorter, and amplitude higher. Faster rates stress neural transmission, particularly through synapses, resulting in longer latencies and lower amplitudes. However, the slower the rate, the longer it takes to acquire the data which may compromise patient cooperation. The optimal stimulation rate must be a compromise between evoked potential morphology and speed of acquisition. In some laboratories, evoked potentials will be obtained with a "fast" rate initially. If the evoked potential is normal at this rate, the test is complete. However, if it is abnormal, the evoked potential will be repeated at a slower rate. Occasionally, an evoked potential is normal with the slow rate, but abnormal with fast rate. How such a test is interpreted is controversial. Some would interpret an evoked potential as normal if it is normal at any stimulation rate. On the other hand, some would interpret an evoked potential abnormal if it is abnormal at any stimulation rate. The author's practice is the former (Figures 1.3A and B).

Repetitions

The number of repetitions refers to the number of evoked responses that must be averaged to produce a reliable evoked potential. The smaller the amplitude of the evoked potential and higher the amplitude of noise (low signal-to-noise ratio), the more repetitions will be needed. The number of repetitions needed is reduced if the signal-to-noise ratio is improved. To some extent this can be done by increasing stimulus intensity and duration and reducing noise. Higher number of repetitions leads to better evoked potential waveform morphology and reproducibility (Figures 1.4A–E). The number of repetitions that are recommended for each type of evoked potentials modality will be discussed in the respective chapters.

Replication

Replication should not be confused with repetitions. Whenever an evoked potential is obtained, it must be reproduced at least once to ensure that the waveforms recorded are reproducible. This is known as replication of the evoked potential. When evoked potentials are not very reproducible, more than one replication may be necessary to confirm the presence of low amplitude waveforms. Most modern evoked potential machines acquire two repetitions simultaneously; that is, alternate stimuli are used to create two different averages.

Recording Methodology

The methods used for recording evoked potentials vary to some degree depending on the evoked potential type. However, there are many aspects of recording that are similar, such as recording electrodes, averaging, and postacquisition signal processing.

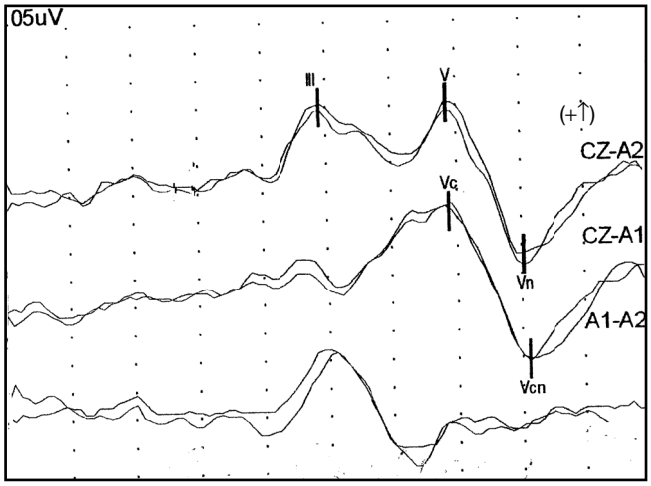
Electrodes

Different types of electrodes can be used to record evoked potentials. Any electrode used should have certain properties that will allow reliable data acquisition.

Properties

Recording electrodes must be able to conduct neural signals without distortion. They must be made of material that resists polarization and does not interact with skin or other human tissue with which it makes contact. Electrodes coated with gold, platinum, or silver coated with silver chloride are most often used. Periodically the electrode's resistance

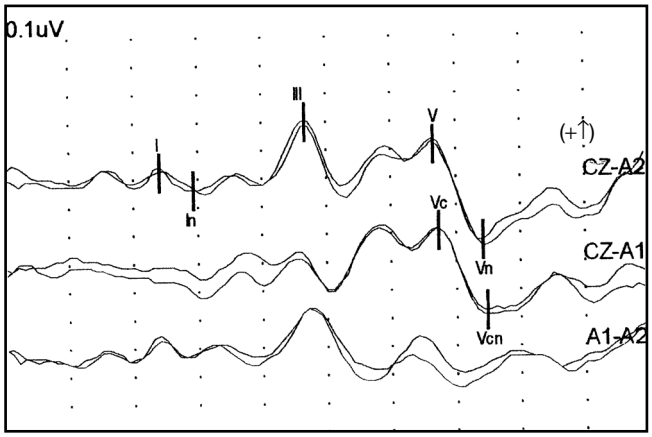
Age: 49 years
Sex: Male
Filters: 150–3,000 Hz
Ear inserts (add 0.9 ms): Yes
Side: Right
Click polarity: Rarefaction
Stimulation intensity: 70 dBnHL
Masking intensity: 40 dBnHL
Number of repetitions: 2,000



(A)
Stimulation rate: 51.1/s
Scale: Amplitude = 0.05 μV/div; Latency = 1 ms/div

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
I	N/A	N/A (I–In)
III	4.88	
V	6.84	0.27 (V–Vn)
Vc	6.86	
		N/A (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	N/A
I–III	N/A
III–Vc	1.98



(B)
Stimulation rate: 11.1/s
Scale: Amplitude = 0.1 μV/div; Latency = 1 ms/div

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
I	2.40	0.07 (I–In)
III	4.66	
V	6.64	0.35 (V–Vn)
Vc	6.72	
		5.0 (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	4.32
I–III	2.26
III–Vc	2.06

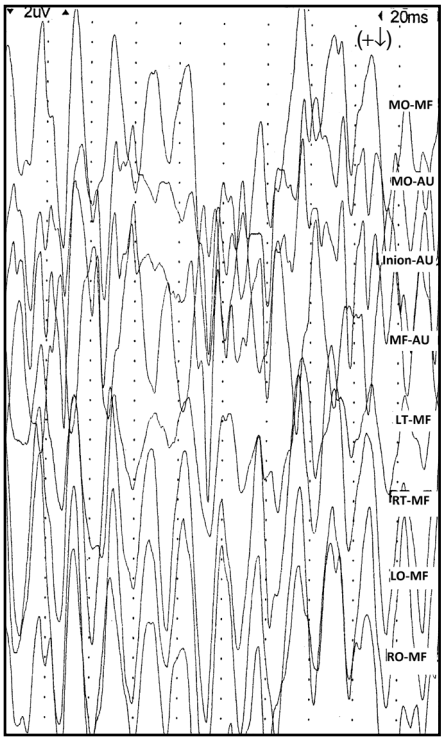
Discussion: Faster stimulation rates can cause degradation in waveform morphology, loss of amplitude, and prolongation of latency. A BAEP obtained with a fast stimulation rate of 51.1/s is shown (A). Notice that the wave I is difficult to identify, despite the sensitivity being set at 0.05 μV/div. In the same patient, when the rate is slowed to 11.1/s (B), the wave I is clearly seen despite the sensitivity being lower (0.1 μV/div). Additionally, the wave V latency is shorter with the slower rate. It is the author's practice to consider a study normal if it is normal at any stimulation rate.

BAEP, brainstem auditory evoked potential.

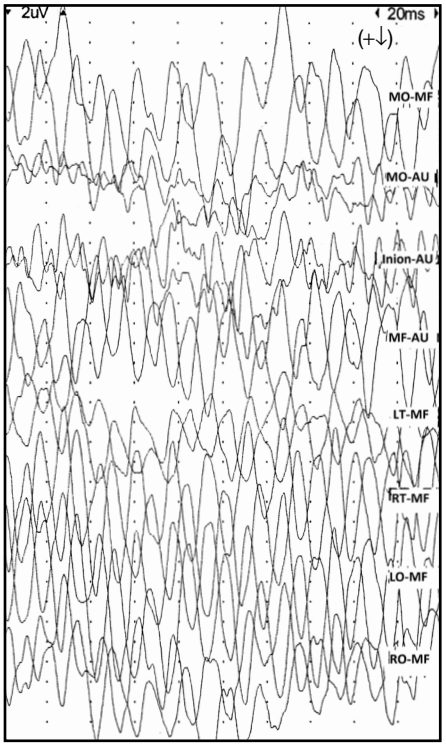
Figure 1.3 (A and B) Effect of stimulation rate on BAEP waveforms.

Age: 43 years
Sex: Male
Stimulation rate: 2.1/s
Filters: A = 1–100 Hz; B = 10–100 Hz; C = 1–30 Hz
Preauricular–preauricular distance: 38 cm
Scale: Amplitude = 2 μV/div; Latency = 20 ms/div
Eye: Right
Visual angle: 30′
Visual acuity: 20/20
Corrective lenses: Yes

(A)
Number of repetitions: 1



(B)
Number of repetitions: 10



(C)
Number of repetitions: 50

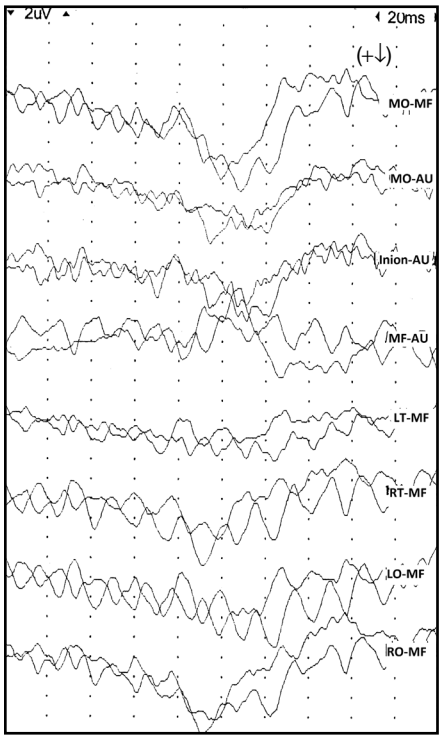
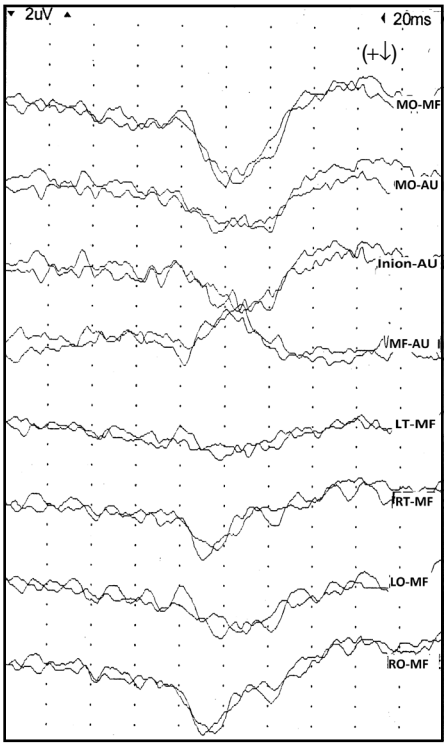
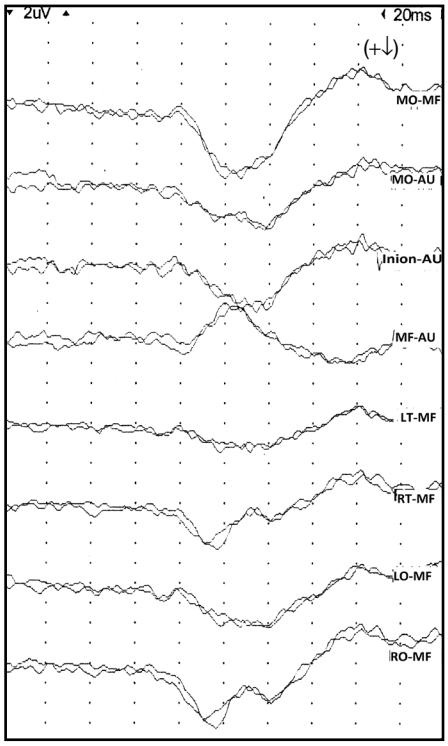


Figure 1.4 (A–E) Effect of number of repetitions on VEP waveforms. (*continued*)

(D)
Number of repetitions: 100



(E)
Number of repetitions: 200



Discussion: This PRVEP shows the utility of increasing repetitions. In Figure A, only one repetition is shown. Figures B, C, D, and E have 10, 50, 100, and 200 repetitions, respectively. With 1 and 10 repetitions, the P100 waveform cannot be identified. With 50 repetitions, the P100 waveform can be identified, but has poor morphology and reproducibility. As the number of repetitions is increased to 100, a much more clearly defined P100 waveform is seen, and this changes only slightly with 200 repetitions. When the evoked potential waveform ceases to change with additional repetitions, averaging is adequate.

PRVEP, pattern reversal visual evoked potential; VEP, visual evoked potential.

Figure 1.4 (A–E) (*continued*)

must be checked. This is the opposition to direct current flow and is measured with an ohmmeter. Electrode resistance should be no more than a few ohms, and if it is very high, a breach in the integrity of the electrode should be suspected. Electrode impedance is the opposition to AC flow. Rather than measuring the integrity of the electrode, impedance evaluates the connection of the electrode to skin or soft tissue and is measured by an impedance meter. Electrode impedance should be below 5,000 Ω (4). Higher impedances degrade the ability of the amplifier to average low amplitude signals.

Types

Surface and needle electrodes can be used to record evoked potential signals. Electroencephalogram (EEG) cup electrodes are the type of surface electrodes used most often. These electrodes are 5 to 10 mm in diameter. Before electrodes are applied, the skin is prepared with a mild abrasive to remove oils and dead skin. The electrode is attached with collodion or paste depending on the indication of the study. Collodion application takes longer and should be performed in a room with adequate ventilation due to the smell of the chemical. It stays attached to the patient for longer period of time. After the electrode has been attached, the cup is filled with conductive jelly to ensure adequate contact between the electrode and skin. Acetone is used to dissolve the collodion and remove the electrode. Conductive electrode paste can also be used to attach electrodes to skin. This method is much

quicker, however it is not as secure as collodion and electrodes can be dislodged more easily.

Needle electrodes can also be used to record evoked potentials. Because they are more invasive than surface electrodes, needle electrodes are not typically used for outpatient evoked potential studies. They can be applied more quickly than surface electrodes as skin preparation is not necessary. This is useful when evoked potentials are performed in the operating room (OR). Needle electrodes have high impedance which can improve signal quality when the amplifier's input impedance is also high.

Placement

Electrode placement depends on the type of evoked potential being recorded. VEP recording electrodes are placed on the scalp, whereas BAEP electrodes are placed on the scalp and mastoids. SEP electrodes are placed on not only the scalp, but also the neck, spine, and limbs. The exact placement is determined by locating anatomical landmarks. Electrodes placed close to each other are used for recording near-field potentials, while electrodes placed at a distance are better at demonstrating far-field potentials.

Amplifiers

The amplifier is the backbone of any evoked potential recording device. A few basic properties of these amplifiers are presented.

Basics

Amplifiers have the task of taking signals that are of very low amplitude and isolating them from background noise. The signals are then amplified to a degree that can be measured and appropriate calculations are performed. Amplifiers consist of an input board, selector switches, differential amplifier, and filters.

Input board

The input board, sometimes also called the jack box or head box, is a small box that is placed near the patient. Electrodes attached to the patient are plugged into receptacles in this box. The input signals are amplified by the input board before they are transmitted to the main unit of the evoked potential machine. This allows the biologic signal to be amplified before any exogenous noise is introduced as the signal travels through cables. Receptacles in the input board also limit the amount of current that can flow from the machine to the patient, so patients cannot receive electrical shocks from the machine.

Selector switches

Selector switches allow pairing two electrode inputs into the amplifier. This allows the amplifier to compare the signal between the two electrodes. It is with selector switches that recording montages are created.

Differential amplifier

The basic principle of a differential amplifier is that it magnifies and displays the difference between two inputs. Each differential amplifier has two main inputs called Input 1 and Input 2; previously these were also called Grid (G) 1 and G2. Because Input 1 is often close to the site generating the potential of interest, it is also referred to as the Active electrode, whereas Input 2 is referred to as the Reference electrode.

The output of a differential amplifier is the difference between Input 1 (G1, active) and Input 2 (G2, reference) electrodes. Even though one electrode is called "active" and the other "reference," both contribute to the ultimate waveform. The display convention used determines if the waveforms deflect upward or downward. At times, more than one electrode can be linked to create one reference (Input 2, G2) electrode. An example of this would be linking the two ears as a single reference.

Because the differential amplifier displays the difference between two inputs, signals that are similar in both inputs will be subtracted. This is known as rejection of the common mode signal. An example of signal that is often rejected because it is in common mode is ECG artifact. Since the ECG artifact is seen in both electrodes, it is subtracted or rejected. However, if the ECG artifact is of different amplitudes in the two electrodes, only some of it will be rejected, and a low amplitude artifact may be seen in the output. The ability of a differential amplifier to reject common mode signal is measured by the common mode rejection ratio (CMRR). The CMRR is defined as the "ratio of amplifier output produced by a signal applied differentially over the amplifier output produced by the same signal when applied in common mode" (1). Contemporary evoked potential machines should have a CMRR of at least 10,000:1 (4).

Averaging

Neurophysiologic signals such as evoked potentials that have amplitude that is lower than the accompanying noise can only be visualized with averaging (5). Averaging involves adding successive responses and dividing the sum by the number of responses. Since the evoked potential is time locked to the stimulus and always occurs at the same latency while noise is random, averaging allows reduction of noise and emergence of the evoked potential signal. Averaging involves digitization of the analog signal in an analog-to-digital (A/D) converter. The digital signal is averaged and then converted back to analog form for display.

The number of responses that need to be averaged to resolve an evoked potential waveform depends on the amplitude of the waveform of interest versus the amplitude of noise. This relationship is called the signal to noise ratio. As discussed earlier, the lower the signal to noise ratio, the more responses that need to be averaged. If the signal to noise ratio is increased, either by increasing the amplitude of the signal or reducing the noise, fewer responses need to be averaged. Averaging improves the signal to noise ratio by a factor equal to the square root of the number of repetitions averaged. It is a common misperception that averaging increases the amplitude of the signal, which is incorrect. It reduces the amplitude of the noise.

Filters

Evoked potentials contain waveforms of a limited frequency range. Filters are used to eliminate unwanted waveforms that are below and above the frequencies of interest. By eliminating low and high frequency activity that is not of interest, fewer repetitions are needed to resolve low amplitude evoked potential waveforms. Analog filters are applied to the signal before it is digitized.

Analog filters are divided into low- and high-frequency filters (LFFs and HFFs). LFFs reduce the amplitude of low frequency activity, and HFFs similarly affect high frequencies. Filters are further named based on the frequency of sine waves whose amplitude they reduce by a fixed percentage, usually 30%. Thus, a 1 Hz LFF will reduce the amplitude of 1 Hz activity by 30%, and amplitude of activity slower than 1 Hz will be reduced more than 30%. The activity range between the LFF and HFF is referred to as the bandpass. Properties of filters are based on sine waves, and biological signals are not sine waves. It is not possible to determine the exact frequency of evoked potential waveforms, and most evoked potentials contain waveforms of many different frequencies. Consequently, filter settings are intentionally set with a broad bandpass so as not to eliminate any waveform of interest. Filters can also distort the shape of waveforms causing them to appear slightly earlier or later. This is called phase shift; progressively greater LFF cause a phase advance (waveforms appear earlier) and progressively lower HFF cause a phase lag (waveforms appear later) (Figures 1.5A–C).

Another special type of filter affects only a very narrow frequency band. This is known as a notch filter. Most often this is a 60 Hz filter in the US as the electrical AC is at this frequency. In other parts of the world, a 50-Hz band filter is available.

Digital filters are used after the signal has been digitized. Several types of digital filters are available and one that is used occasionally in clinical evoked potentials is called "smoothing" (1). Smoothing uses a computer algorithm to average three to five consecutive data points to help eliminate noise and "smooth" out waveforms. Smoothing can be used more than once on a waveform. However, it should be used sparingly as it can affect waveform morphology (Figures 1.6A–C). Digital filtering, however, does not cause phase shifts.

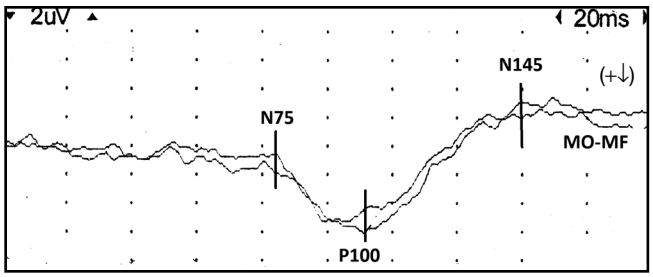
Artifact rejection

Artifact rejection is another technique used to help resolve low-amplitude signals such as evoked potentials. Amplifier input voltage is set so that signals of excessively high voltage that are unlikely to be of interest are automatically rejected and not included in the average. This prevents the average from being contaminated from these high-amplitude signals. The limits of artifact rejection should be set so that signals of interest are not affected. Artifact rejection allows a reduction of the number of responses that need to be averaged. However, if the artifact rejection level is set too low, too many responses will be rejected, increasing the time and responses needed to average.

Interpretation

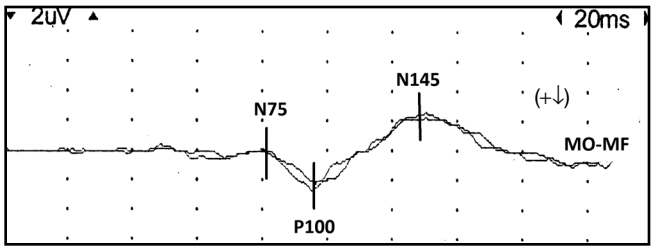
Interpretation of evoked potentials involves a detailed evaluation of the waveforms. This includes determining the presence, morphology, latency, amplitude, and several other features of waveforms.

Age: 43 years
Sex: Male
Stimulation rate: 2.1/s
Filters: A = 1–100 Hz; B = 10–100 Hz; C = 1–30 Hz
Preauricular–preauricular distance: 38 cm
Scale: Amplitude = 2 μV/div; Latency = 20 ms/div
Eye: Right
Number of repetitions: 200
Visual angle: 30′
Visual acuity: 20/20
Corrective lenses: Yes



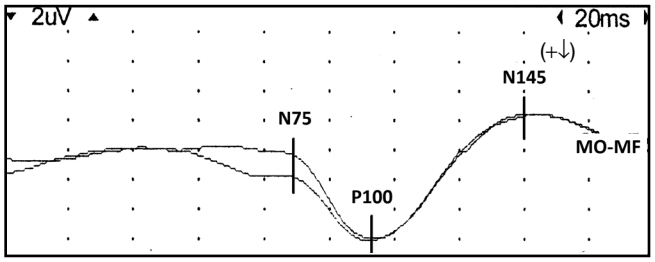
(A)

Absolute Latency			
Derivation MO–MF	N75 (ms)	P100 (ms)	N145 (ms)
A	84.1	112.0	158.3
B	81.3	95.6	128.0
C	88.7	114.5	160.1



(B)

Amplitude			
Derivation MO–MF	N75–P100 (μV)	P100–N145 (μV)	Mean (μV)
A	4.20	8.21	6.21
B	2.20	5.10	3.65
C	5.86	8.34	7.10



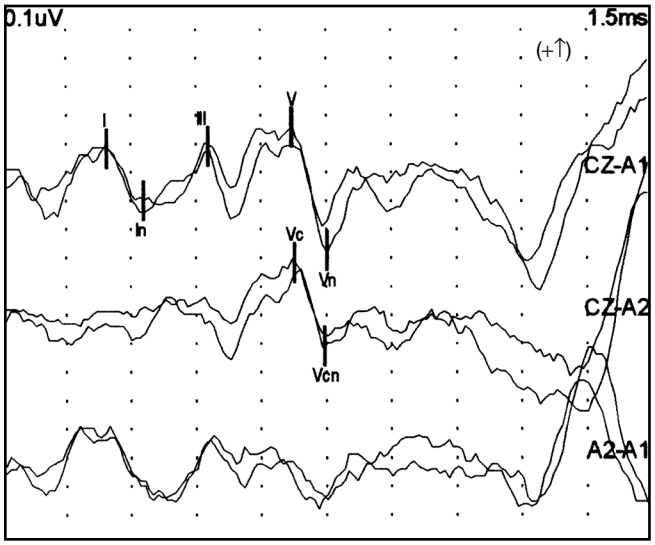
(C)

Discussion: Filters can affect the shape and latency of evoked potential waveforms. In Figure A, a PRVEP with usual filter setting of 1 to 100 Hz is shown. Figure B shows same waveform obtained with the LFF increased to 10 Hz (10–100 Hz). Notice that this reduces the amplitude and shortens the latency of the P100 waveform. Figure C shows the same waveform with the HFF reduced to 30 Hz (1–30 Hz). Because the P100 waveform is a low-frequency waveform, this does not reduce the amplitude but increases the latency. Thus, increasing the LFF causes a phase advance and decreasing the HFF causes a phase delay of the evoked potential waveforms.

HFF, high-frequency filter; LFF, low-frequency filter; PRVEP, pattern reversal visual evoked potential; VEP, visual evoked potential.

Figure 1.5 (A–C) Effect of filter changes on VEP waveforms.

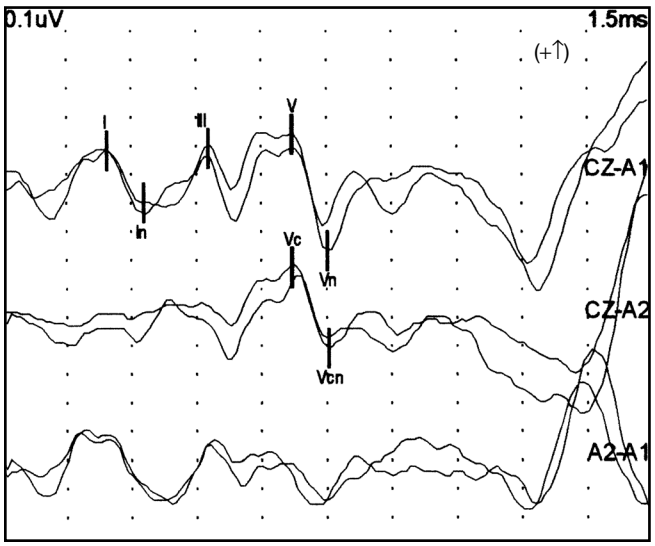
Age: 32 years
Sex: Female
Stimulation rate: 31.1/s
Filters: 150–3,000 Hz
Scale: Amplitude = 0.1 μV/div; Latency = 1.5 ms/div
Ear inserts (add 0.9 ms): Yes
Side: Left
Click polarity: Alternating
Stimulation intensity: 85 dBnHL
Masking intensity: 55 dBnHL
Number of repetitions: 4,000



(A)

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
I	2.43	0.19 (I–In)
III	4.77	
V	6.69	0.44 (V–Vn)
Vc	6.75	
		2.3 (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	4.32
I–III	2.34
III–Vc	1.98

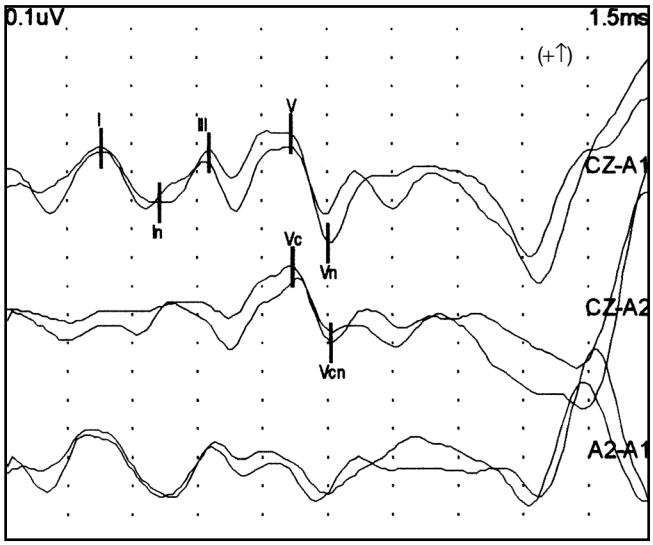


(B)

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
I	2.43	0.19 (I–In)
III	4.77	
V	6.69	0.42 (V–Vn)
Vc	6.69	
		2.2 (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	4.26
I–III	2.34
III–Vc	1.92

Figure 1.6 (A–C) Effect of smoothing filter on BAEP waveforms. (*continued*)



(C)

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
I	2.28	0.20 (I–In)
III	4.77	
V	6.66	0.39 (V–Vn)
Vc	6.69	
		2.0 (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	4.41
I–III	2.49
III–Vc	1.92

Discussion: Excessive smoothing can distort evoked potential waveforms. Figure A shows a BAEP waveform which has not undergone smoothing. Figure B is the same waveform with smoothing done once. Figure C shows the waveform with smoothing performed 10 times. Notice the change in absolute and interpeak latencies. Smoothing does make the waveforms look "cleaner," but that is at the expense of accuracy.

BAEP, brainstem auditory evoked potential.

Figure 1.6 (A-C) (*continued*)

The patient's evoked potential is compared to normative data to determine if an abnormality is present.

Peak Identification

The various evoked potential types used in clinical practice have a typical series of peaks that occur at expected latencies. This allows for nomenclature of the peaks, as discussed earlier. Peaks may be labeled according to their polarity and expected latency (i.e., N20 waveform is a negative peak occurring at approximately 20 ms) or their number in a series (i.e., wave III is the third BAEP waveform). Peak identification is easy when a normal response is present. However, in cases of abnormalities, peak latencies may be highly variable, there may be excessive noise making evoked potential waveforms difficult to discern, and morphology of the waveform may be distorted. There are specific recommendations for evaluating the waveforms for each type of evoked potential, which will be discussed in the respective chapters.

A few basic principles apply to identification of all waveforms. Responses that are difficult to ascertain because of low amplitude may be improved by increasing the stimulation intensity or duration. This is particularly true for SEP. On the other hand, occasionally the stimulation intensity can be too high and extra waveforms are seen that make identification of waveforms of interest difficult. This happens when very high stimulation intensities are used for obtaining BAEP. This results in extra waveforms, which makes identifying waves I to V difficult. Reducing the stimulation intensity can eliminate the extra waveforms, making interpretation easier.

At times instead of a single peak, two smaller peaks may appear. This is known as a bi-fed waveform. When a bi-fed waveform is seen, it may be suggestive of pathology or may be an artifact of

the recording method. An example of the latter can be seen when the P100 waveform is obtained with a midoccipital to mid frontal (MO-MF) derivation. Contributions from the N105 waveform recorded from the MF electrode and the P100 waveform recorded from the MO electrode are added together to create the bi-fed waveform. This bi-fed waveform, also called W-shaped waveform, can be resolved by changing the reference electrode to Ai-Ac (linked ears). When the bi-fed waveform cannot be resolved with montage changes, a decision needs to be made how latency and amplitude measurements will be obtained. Latency can be measured to the first peak, to the second peak, or to the average of the two peaks. Similarly, amplitude can be measured of the first or second peak. Regardless of which method is used, it should be consistent with laboratory protocol.

Excessive noise can also make peak identification difficult. An attempt should be made to reduce the noise by having the patient relax or sleep. The noise can be measured by averaging without stimulating. If a flat baseline is not obtained with this method after a standard number of repetitions, the evoked potentials may be difficult to resolve. The number of repetitions obtained can be increased; however the signal to noise ratio increases by a factor of the square root of the number of repetitions. This makes increasingly higher number of repetitions of diminishing utility.

Modern evoked potential equipment automatically tags waveforms based on a preprogrammed algorithm. This works reasonably well when the response is normal. However, when the response is abnormal, the automated peak labeling may be incorrect. Similarly, evoked potential technologists label waveforms they think correspond to waveforms of interest. Experienced technologists are often correct, but even they may be inaccurate with more complex studies (Figure 1.7). It behooves the interpreter to double check that the waveforms are appropriately tagged.

Latency

Latency measurement is the most important measure of evoked potential waveforms. Two main types of latencies can be determined.

Absolute latency

The absolute latency, also referred to as the peak latency, is measured from the start of the stimulus to peak of the waveform of interest. The onset latency is the time from stimulus onset to the start of the waveform. This latter latency measure is not routinely used as the onset of a waveform is much harder to determine than the peak (Figure 1.8).

The absolute latency of a waveform is the time an impulse takes to travel from the point of stimulation to the generator of the waveform of interest. Because the stimulus is applied to end organ, absolute latency measures conduction in the peripheral and central nervous system (or in the case of VEP, the retina). A lesion of the peripheral nervous system, such as demyelination of a peripheral nerve, can cause the absolute latency to be prolonged.

Interpeak latency

Interpeak latency (IPL) is the latency between two peaks of the same evoked potential. It represents the time an impulse takes to travel between the presumed generators of the waveforms. IPLs are useful in eliminating the peripheral nervous system contribution to the latency. If the IPL between two waveforms that are both in the central nervous system is determined, only central nervous system conduction is measured. This is particularly helpful in SEP and BAEP. In SEP, the IPL between the upper and lower spinal cord (for upper and lower extremity SEP) and brain can determine central conduction time (CCT). IPL measurement is preferred to absolute latency measurements as they are less variable and not influenced by peripheral nervous system pathology (Figure 1.8).

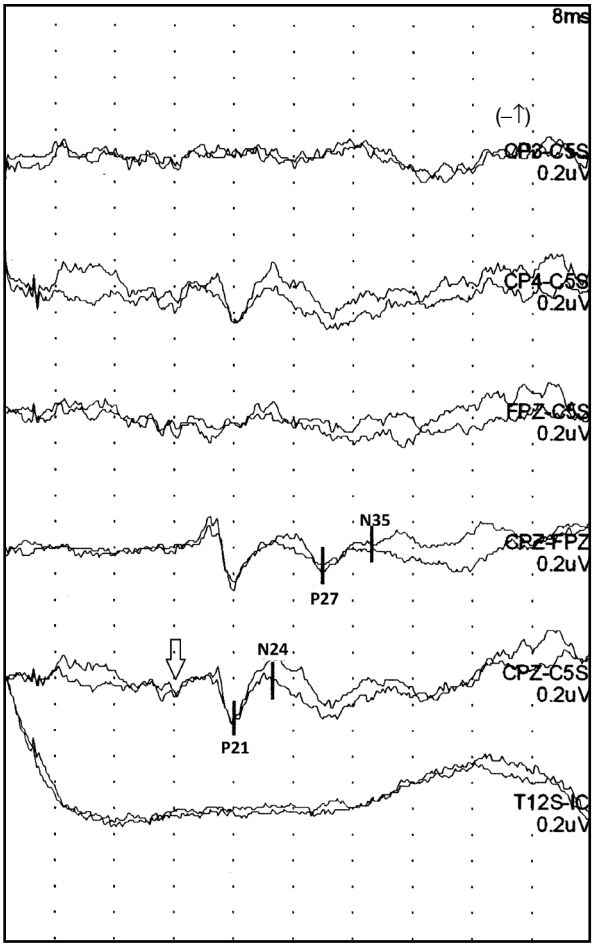
Amplitude

As with latency measurements, amplitude of waveforms can be measured in several ways. Amplitude abnormalities are not as reliable as latency abnormalities. Evoked potentials are seldom interpreted as abnormal if only amplitude abnormalities exist.

Peak to peak amplitude

Peak to peak amplitude is the most commonly used amplitude measurement. It is a measure of the voltage difference between successive peaks of opposite polarity. The amplitude of the ascending limb, descending limb, or the average of both is

Age: 18 years
Sex: Male
Stimulation rate: 5.7/s
Filters: 30–3,000 Hz
Scale: Amplitude = 0.2 µV/div; Latency = 8 ms/div
Side: Right
Stimulation duration: 0.2 ms
Stimulation intensity: 30.9 mA
Number of repetitions: 1,503



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
LP	N/A	
P21 (31)	32.0	
N24 (34)	37.1	
P27 (37)	43.9	0.18 (P27–N35)
N35 (45)	50.4	

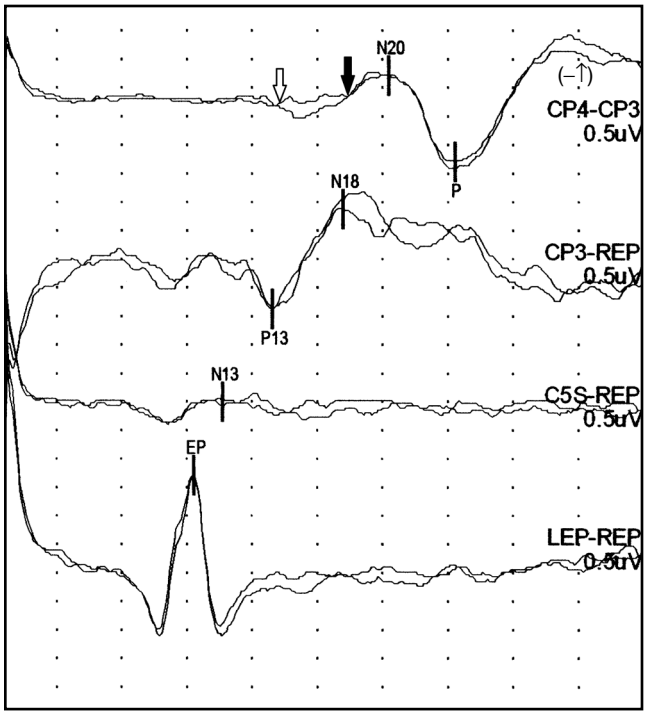
Interpeak Latencies	
Waveforms	**Latency (ms)**
LP–P27	N/A

Discussion: Before looking at waveform latencies, the interpreting physician must first evaluate the waveforms and confirm that they have been properly tagged. This is a peroneal nerve SEP, and absolute latencies of peroneal SEP are 10 ms less than tibial nerve SEP. The waveforms are correspondingly called P21, N24, and P27. In some laboratories, for simplicity, the nomenclature for tibial nerve SEP is retained for peroneal nerve SEP, that is, the previously noted waveforms are called P31 waveform, N34 waveform, and P37 waveform. A PF waveform is not recorded as that is the site of stimulation. All waveforms have been incorrectly tagged. The waveform tagged P21 is actually the P27. Notice that this waveform is seen not only in the CPz–C5S and CP4–C5S derivations, it is also seen in the CPz–FPz derivation. It is not seen in the FPz–C5S and CP3–C5S derivations. If this waveform was a subcortical P21, it should not have been seen in the CPz–FPz derivation (it would have been in "common mode" in both electrodes), and it should have been seen in the FPz–C5S and CP3–C5S derivations. The waveform marked with the arrow is the P21, and it follows the properties of the subcortical response discussed earlier. If this was not noticed and the absolute latencies relied upon as provided, the interpretation for this study would have been that it was abnormal due to prolongation of the P27 waveform. In fact, the interpretation should be that it is a normal study since the latency of the P27 waveform is actually 32.0 ms (upper limit of normal for P27 waveform is 37.0 ms).

SEP, somatosensory evoked potential.

Figure 1.7 Automated tagging of peroneal nerve SEP waveforms.

Age: 30 years
Sex: Male
Stimulation rate: 5.7/s
Filters: 30–1,500 Hz
Scale: Amplitude = 0.5 µV/div; Latency = 3 ms/div
Side: Left
Stimulation duration: 0.2 ms
Stimulation intensity: 10.1 mA
Number of repetitions: 750
Median nerve conduction velocity (median nerve to EP waveform): 52 m/s



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
EP	9.3	
N13	10.6	
P13	12.9	
N18	16.1	1.78 (P13–N18)
N20	18.2	1.52 (N20–P22)

Interpeak Latencies	
Waveforms	**Latency (ms)**
EP–N20	8.90
EP–P13	3.60
P13–N20	5.30

Discussion: Waveform latencies can be determined either to their onset or peak. Peak latencies are used more often in evoked potentials as onset may be difficult to identify. In this example, the N20 waveform onset latency can be either where the light or dark arrow is placed. The peak latency is where the N20 waveform is tagged. More important than peak (or absolute) latencies are IPL. IPLs are more accurate than absolute latencies in determining central conduction.

IPL, interpeak latency; SEP, somatosensory evoked potential.

Figure 1.8 Latency measurements of SEP waveforms.

determined (Figure 1.9). Whichever method is used, it is important to be consistent within a laboratory and the normative data must have been obtained with the same method.

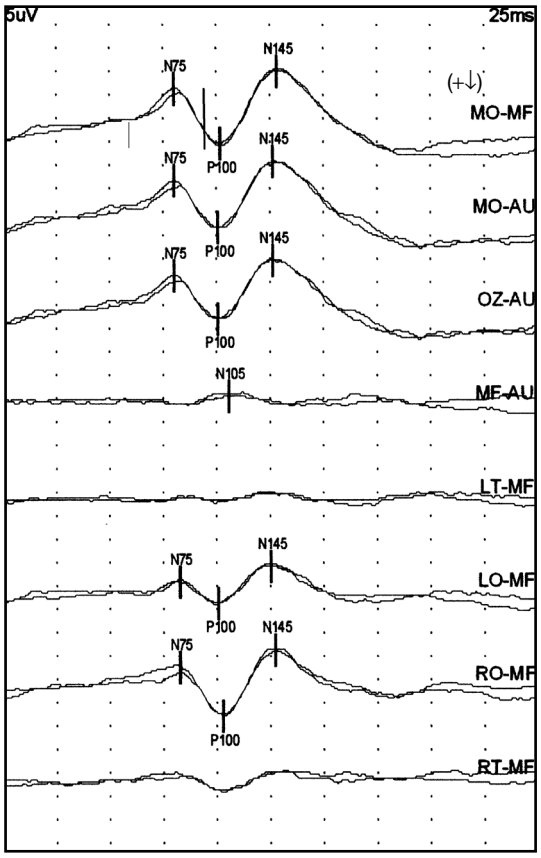
Baseline to peak amplitude

The baseline to peak amplitude is the voltage from the baseline to the peak of the waveform of interest. The baseline is the immediate post stimulus period of the evoked potential (Figure 1.9). This measurement may be difficult to determine as the baseline may not be horizontal.

Amplitude ratio

The ratio of the peak to peak amplitude of two waveforms of the same evoked potential can be determined and is thought to be a more sensitive amplitude measurement than peak to peak amplitude of a single

Age: 39 years
Sex: Female
Stimulation rate: 3.9/s
Filters: 1–100 Hz
Preauricular–preauricular distance: 33 cm
Scale: Amplitude = 5 μV/div; Latency = 25 ms/div
Eye: Right
Number of repetitions: 100
Visual angle: 30′
Visual acuity: 20/25
Corrective lenses: No



Absolute Latency				
Derivation	N75 (ms)	P100 (ms)	N105 (ms)	N145 (ms)
MO–MF	80.0	102.0		128.0
MO–AU	80.0	101.0		126.0
Oz–AU	80.0	101.0		126.0
MF–AU			106.0	
LO–MF	82.5	101.0		125.0
RO–MF	82.5	103.0		127.0

Amplitude			
Derivation	N75–P100 (μV)	P100–N145 (μV)	Mean (μV)
MO–MF	12.2	16.1	14.2
MO–AU	10.5	14.6	12.6
Oz–AU	9.68	13.0	11.3
LO–MF	4.95	8.55	6.8
RO–MF	10.7	14.2	12.5

P100 Amplitude Ratio	
Location	Ratio
OS–OD	1.2
LO–RO	1.8

Discussion: Amplitude of a waveform can be measured from baseline to peak or from peak to peak. The latter is used more often in evoked potentials since identifying peaks is more reliable than identifying the baseline. In the example shown, the baseline to peak (narrow line) P100 waveform amplitude is not as reliable as the N75–P100 waveform peak to peak amplitude (broad line). Peak to peak amplitudes can be measured for the descending or ascending limb of the peak, or it can be an average of the two. The above example displays amplitudes of the descending and ascending limb, but it is the average that is used in the author's laboratory. Amplitude ratios are used in PRVEP to compare parasagittal P100 waveforms (those obtained from LO–MF and RO–MF derivations) and the P100 waveforms obtained after left and right eye stimulation. In the above example, the parasagittal waveform amplitude ratio is within normal limits, as is left and right eye P100 waveform amplitude ratio (PRVEP to left eye stimulation not shown).

PRVEP, pattern reversal visual evoked potential; VEP, visual evoked potential.

Figure 1.9 Amplitude measurements of VEP waveforms.

waveform. This is commonly used in BAEPs where wave V/I amplitude ratio is measured. Amplitude ratios can also be used to compare the same waveform obtained after stimulation of the left and right side or recorded from different locations. This is done with PRVEP where the P100 waveform can be compared after left and right sided stimulation. The P100 waveform recorded from parasagittal electrodes can also be compared (Figure 1.9).

Other Measurements

It is also important to review other measures that are assessed in the evoked potentials laboratory which are not directly related to the evoked potential. These include measures such as visual acuity for PRVEP, hearing thresholds for BAEP, and peripheral nerve conduction velocities for SEP. These measures help in interpreting the evoked potential since they can provide clues as to whether pathology exists in the end organ being stimulated or the peripheral nervous system. Impaired visual acuity can lead to P100 waveform latency prolongation, hearing loss can cause prolonged absolute latency of wave I of the BAEP, and slowed conduction velocity can affect SEP waveforms.

Variability

Evoked potentials obtained with similar methodology may appear different within the same patient when recorded at different times, and between patients the variability may be even more. There are many reasons for this variability.

Intraindividual variability

Many factors within a patient may affect an evoked potential. Foremost is the attention level. Cortical responses are of higher amplitude when the patient is awake than if they are drowsy or asleep. If the patient is awake when the study is obtained on one side and falls asleep when the other side is acquired, there may be considerable variability of the evoked potential (6). This is seen most remarkably in tibial nerve SEP (Figures 1.10A and B). If the background activity or noise increases, the evoked potential may become more difficult to visualize as the signal to noise ratio is lower. A drop in blood pressure may make the amplitude of the evoked potential lower, which also reduces the signal to noise ratio. This is seldom seen in an outpatient setting, but may occur when evoked potentials are performed in an intensive care unit and OR. When there are lesions of the cerebral cortex, evoked potentials may be more variable.

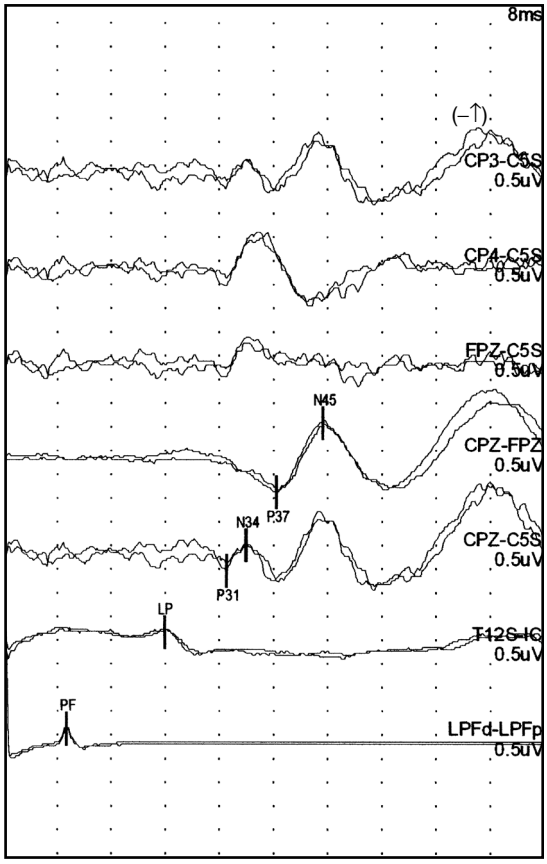
Interindividual variability

Evoked potentials can vary considerably between individuals. Sex and body or head size, which are related, can have a significant effect on evoked potential waveform latency. Age can also have an effect on evoked potentials. The biggest change is from infancy to maturity, but changes can also occur with old age. Anatomical variability of neural structures may also cause morphological differences in the evoked potentials. An example of this is the P37 cortical waveform obtained after tibial nerve stimulation. Because the leg somatosensory cortex is near the vertex, the P37 waveform is typically best recorded contralateral to the side of waveform generation (ipsilateral to side of stimulation since dorsal column pathway fibers decussate in the medulla). However, occasionally the P37 waveform is better recorded over the vertex or ipsilateral to site of waveform generation.

Normal Evoked Potentials

When interpreting an evoked potential study, various aspects of the data are compared to normative values. Details of what to evaluate for each modality will be presented in the respective chapters. Normative data are obtained by performing evoked potentials on a group of individuals who do not have neurologic disease. It is important to include both sexes and the spectrum of ages that will be evaluated. At the extremes of ages, it is useful to have separate norms. The data are evaluated to determine if it is normally distributed. If it is, the mean values for latency and amplitude of the waveforms of interest have to be calculated. The upper limit of normal is then defined as the mean value plus 2.5 or 3 standard deviations above the mean. At least 20 individuals should be tested to determine the mean latency and amplitude values. If the data are not normally distributed, the percentile method is used, which indicates the probability that the evoked potential from the control group will be similar to the acquired evoked potential. In the latter method, about 100 subjects must be studied to obtain normative data. Ideally, all evoked potential laboratories should obtain their own normative data by using methodology that is similar to that which will be used for performing clinical studies. However, obtaining normative data is difficult, especially for small laboratories. In these instances, it is acceptable to use published normative data if clinical studies are done using

Age: 43 years
Sex: Male
Stimulation rate: 5.7/s
Filters: 30–3,000 Hz
Scale: Amplitude = 0.5 μV/div; Latency = 8 ms/div

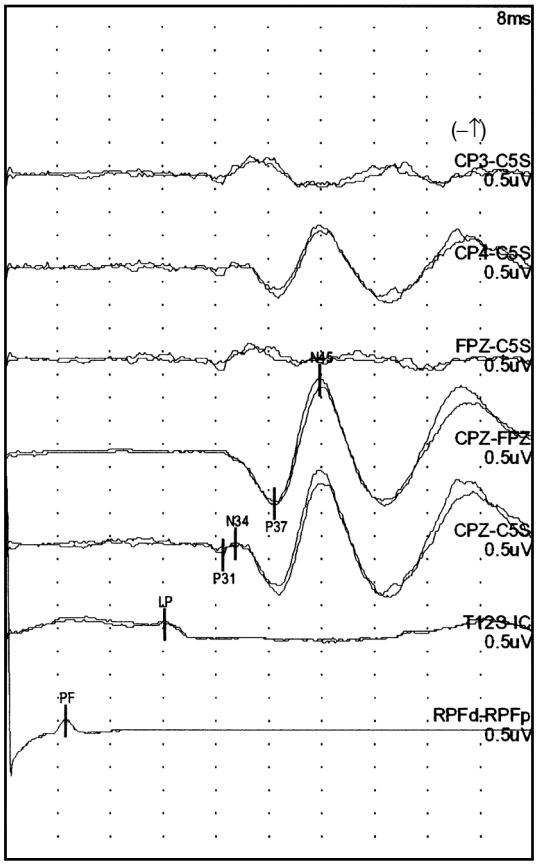


(A)
Side: Left
Stimulation duration: 0.2 ms
Stimulation intensity: 26.6 mA
Number of repetitions: 2,006
Tibial nerve conduction velocity (tibial nerve to T12S): 41 m/s

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
PF	9.3	
LP	23.9	
P31	32.9	
N34	35.9	
P37	40.3	1.52 (P37–N45)

Interpeak Latencies	
Waveforms	**Latency (ms)**
PF–P37	31.0
LP–P37	16.4

Figure 1.10 (A and B) Effect of attention on tibial nerve SEP waveforms. (*continued*)



(B)
Side: Right
Stimulation duration: 0.2 ms
Stimulation intensity: 25.0 mA
Number of repetitions: 3,000
Tibial nerve conduction velocity (tibial nerve to T12S): 41 m/s

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
PF	9.1	
LP	24.1	
P31	32.9	
N34	34.9	
P37	40.8	2.75 (P37–N45)

Interpeak Latencies	
Waveforms	**Latency (ms)**
PF–P37	31.7
LP–P37	16.7

Discussion: State change of the patient, such as waking up or falling asleep, can affect evoked potential waveforms, particularly tibial nerve SEP. In this example, right tibial nerve SEP (B) was performed first when the patient was fully awake. When left tibial nerve SEP stimulation was started (A), the patient was becoming drowsy. Thus, the left tibial nerve SEP was obtained when the patient was not as alert as he was for the right tibial nerve SEP. Notice that the cortical P37 waveform is of higher amplitude with right sided stimulation, when the patient was fully awake. The absolute and interpeak latencies are normal, but the P37 waveform amplitude is asymmetric. This finding alone does not make this study abnormal.

SEP, somatosensory evoked potential.

Figure 1.10 (A and B) (*continued*)

the same methodology as the reference laboratory. Additionally, a few studies on normal individuals should be done using the reference laboratory's methodology to confirm that normal results are obtained.

In clinical evoked potentials interpretation, the most important variable to analyze is the latency. For each type of evoked potential, a series of IPL and absolute latencies should be compared to normative data. In BAEP and SEP, IPLs are more important than absolute latencies, but for VEP the absolute latencies are evaluated. Even if latencies are within normal limits, they should be compared from side to side to determine if an asymmetry exists. Asymmetric latencies may also suggest an abnormality.

The amplitude of waveforms should also be determined. As with latency, there are some waveforms for each type of evoked potential for which amplitude is routinely determined. Most laboratories do not use peak to peak or baseline to peak amplitude to determine normalcy of waveform. When amplitude is used, it is often the amplitude ratio that is evaluated. The amplitude ratio may be of different waveforms of the same evoked potential (wave V/I ratio of the BAEP), the same waveform obtained after contralateral stimulation (ratio of P100 waveform amplitude obtained after left and right eye stimulation), or the same waveform obtained with different recording derivations (ratio of the left and right parasagittal P100 waveform amplitude).

Morphology and topography of the waveform are generally not used in determining whether an evoked potential study is normal. As noted earlier, both of these are highly variable between individuals. Often changing montages and recording from different electrodes to compensate for variable topography will result in more "normal" appearing waveforms.

Abnormal Evoked Potentials

As noted earlier, the most significant evoked potential abnormality is latency prolongation. Amplitude and shape of the waveform should also be evaluated, but these are seldom used as the sole criteria for abnormality. The abnormalities seen in evoked potentials can be used to localize the site of the potential lesion.

Latency prolongation

Prolongation of the latency of a waveform implies that there is slowing of the conduction velocity of the neural pathways from the point of stimulation to the neural generator of the waveform. The slowing is often caused by a lesion along the pathway. When recording evoked potentials, the slowing of interest is that which affects the central nervous system. However, when absolute latencies are evaluated, peripheral nerve conduction is also measured. For example, a delayed N20 waveform absolute latency of the median nerve SEP may be due to demyelinating peripheral neuropathy or a brainstem lesion affecting the medial lemniscus (Figure 1.11). Similarly, prolongation of the P100 waveform of the PRVEP may be due to ocular problems or an optic chiasm lesion.

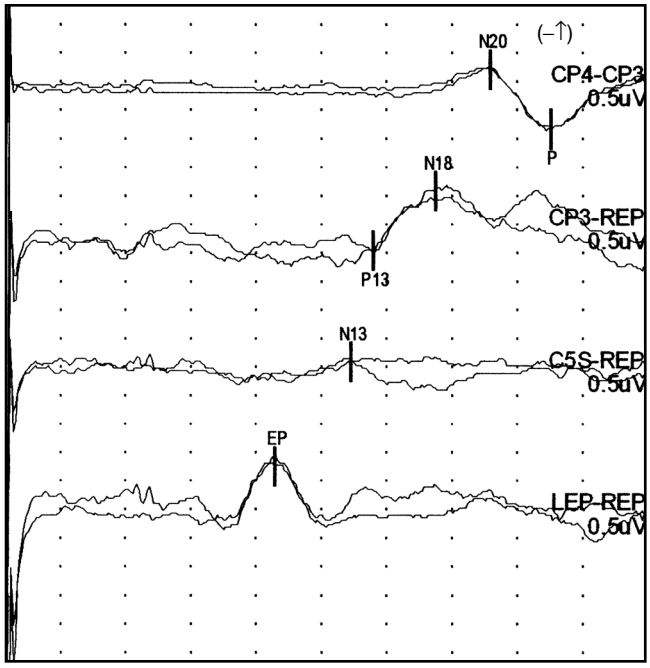
IPL assessments are much more accurate for evaluating the central nervous system. These measures allow assessment of neural pathways between generators of two waveforms. For example, for median nerve SEPs, the waves EP–N20 (EP to N20 waveform) IPL assesses neural pathways between the brachial plexus and the contralateral somatosensory cortex and the waves P14 to N20 IPL provides an assessment of the fibers between the nucleus cuneatus and the contralateral somatosensory cortex. Diseases of the peripheral nervous system are much less likely to affect IPL (Figure 1.11). Similarly, BAEP waves I to V IPL allows assessment of the auditory pathway after removing the contributions of the peripheral hearing apparatus. It is not unusual to see a prolonged wave V absolute latency with a normal wave I to V IPL. This suggests a lesion at or before the cochlea and not of the central nervous system. The VEP is unique in that only the P100 waveform is measured, so IPL cannot be determined.

Absolute latencies and IPLs are compared to normative data to see if they exceed the upper limit of normal latency measures. Even if these measurements do not exceed the upper limits of normal, it is useful to compare latencies from side to side. If greater than maximal allowable asymmetry is noted, the side with slower conduction may be abnormal (Figures 1.12A and B).

Amplitude reduction

A reduction in the amplitude of evoked potential peaks is most often accompanied by latency prolongation. The lower amplitude can be explained by temporal dispersion if conduction is slowed. However, at times amplitude reduction is noted without latency prolongation (Figures 1.13A and B). Whereas this may imply axonal loss in the pathway being tested, it may also be due to

Age: 60 years
Sex: Male
Stimulation rate: 5.7/s
Filters: 30–1,500 Hz
Scale: Amplitude = 0.5 µV/div; Latency = 3 ms/div
Side: Left
Stimulation duration: 0.2 ms
Stimulation intensity: 21.9 mA
Number of repetitions: 1,000
Median nerve conduction velocity (median nerve to EP waveform): 39 m/s



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
EP	12.8	
N13	16.3	
P13	17.3	
N18	20.2	1.09 (P13–N18)
N20	22.7	1.07 (N20–P22)

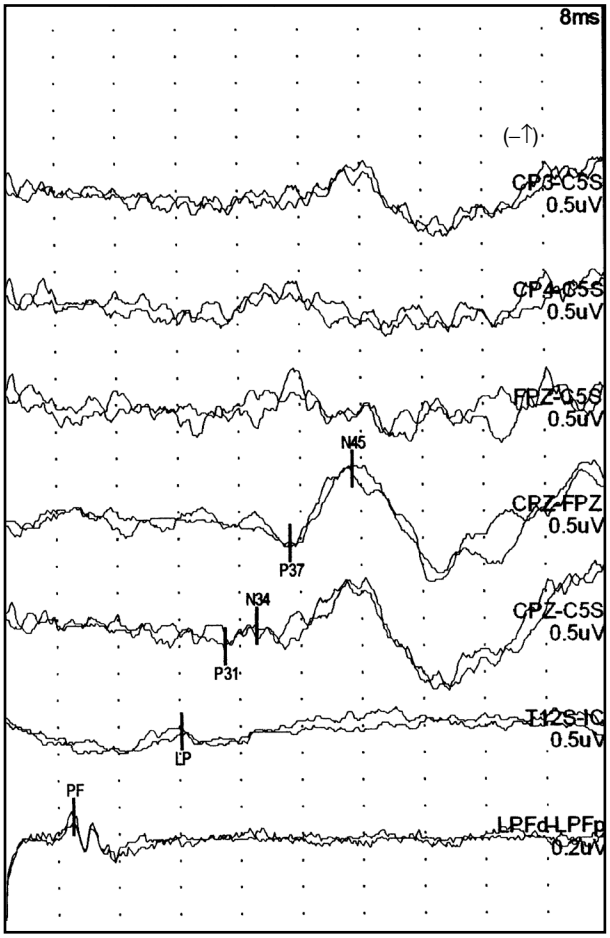
Interpeak Latencies	
Waveforms	**Latency (ms)**
EP–N20	9.90
EP–P13	4.50
P13–N20	5.40

Discussion: Absolute latencies are a measure of both peripheral and central conduction velocity. IPLs are a more accurate method of evaluating central nervous system conduction. In this example, absolute latencies of all waveforms, including the EP and N20 waveforms, are prolonged. However, when the waves EP–N20 IPL and other IPLs are evaluated, it is evident that the absolute latency prolongation is due to a peripheral nervous system process. This is further supported by what appears to be a slowing of median nerve conduction velocity. It is cautioned that supramaximal stimulation is not applied to the peripheral nerve in the evoked potentials laboratory, and so the conduction velocity should be interpreted with the understanding that all nerve fibers may not have been stimulated.

IPL, interpeak latency; SEP, somatosensory evoked potential.

Figure 1.11 Latency prolongations of median nerve SEP waveforms.

Age: 41 years
Sex: Female
Stimulation rate: 5.7/s
Filters: 30–3,000 Hz
Scale: Amplitude = 0.5 μV/div; Latency = 8 ms/div

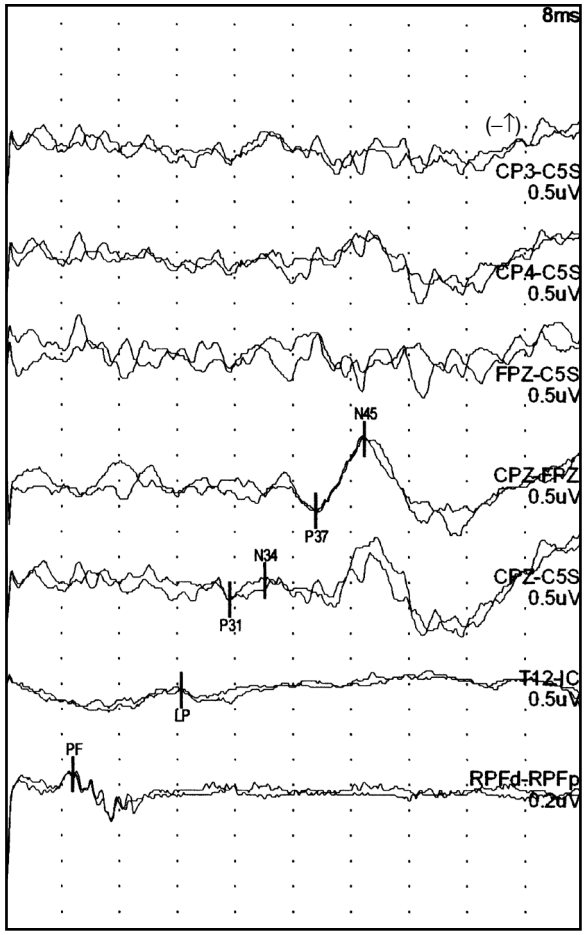


(A)
Side: Left
Stimulation duration: 0.3 ms
Stimulation intensity: 24.3 mA
Number of repetitions: 1,500
Tibial nerve conduction velocity (tibial nerve to T12S): 43 m/s

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
PF	9.9	
LP	24.2	
P31	29.9	
N34	34.0	
P37	38.6	1.45 (P37–N45)

Interpeak Latencies	
Waveforms	**Latency (ms)**
PF–P37	28.7
LP–P37	14.4

Figure 1.12 (A and B) Latency asymmetries of tibial nerve SEP waveforms. (*continued*)



(B)
Side: Right
Stimulation duration: 0.3 ms
Stimulation intensity: 29.0 mA
Number of repetitions: 1,500
Tibial nerve conduction velocity (tibial nerve to T12S): 43 m/s

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
PF	9.4	
LP	24.4	
P31	31.2	
N34	36.0	
P37	43.0	1.49 (P37–N45)

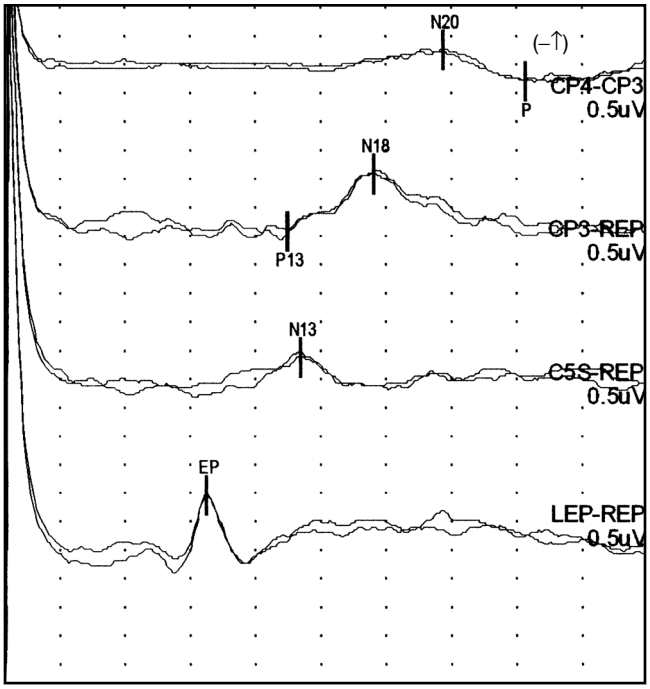
Interpeak Latencies	
Waveforms	**Latency (ms)**
PF–P37	33.6
LP–P37	18.6

Discussion: Absolute and interpeak latencies are compared to normative data to determine if pathology exists. Additionally, latencies should be compared from side to side in the same patient. At times, latencies can be within normal limits, but a significant difference is present between the two sides. If this latency difference is beyond the upper limit of normal, even if the latencies themselves are within normal limits, the study is considered abnormal. In this example, left (A) and right (B) tibial nerve SEP are shown. The waves LP–P37 IPL are asymmetric (14.4 ms vs. 18.6 ms), with a shorter latency after left-sided stimulation. Both IPLs, however, are within normal limits. Because of this asymmetry, this study is considered abnormal.

IPL, interpeak latency; SEP, somatosensory evoked potential.

Figure 1.12 (A and B) (*continued*)

Age: 56 years
Sex: Female
Stimulation rate: 5.7/s
Filters: 30–1,500 Hz
Scale: Amplitude = 0.5 μV/div; Latency = 3 ms/div

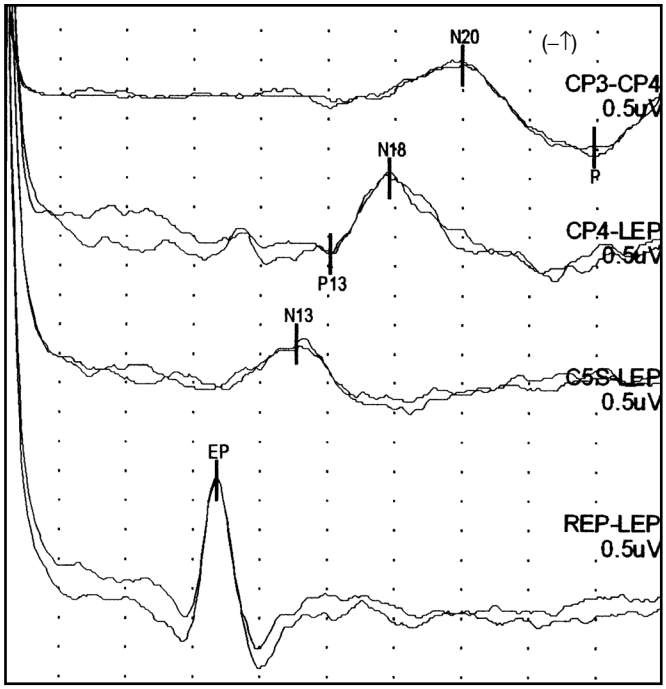


(A)
Side: Left
Stimulation duration: 0.2 ms
Stimulation intensity: 12.5 mA
Number of repetitions: 1,500
Median nerve conduction velocity (median nerve to EP waveform): 60 m/s

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
EP	9.72	
N13	14.0	
P13	13.4	
N18	17.4	1.04 (P13–N18)
N20	20.6	0.57 (N20–P22)

Interpeak Latencies	
Waveforms	**Latency (ms)**
EP–N20	10.88
EP–P13	3.68
P13–N20	7.20

Figure 1.13 (A and B) Low amplitudes of median nerve SEP waveforms. (*continued*)



(B)
Side: Right
Stimulation duration: 0.2 ms
Stimulation intensity: 14.9 mA
Number of repetitions: 1,002
Median nerve conduction velocity (median nerve to EP waveform):

Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (μV)**
EP	10.0	
N13	13.6	
P13	15.1	
N18	17.7	1.33 (P13–N18)
N20	20.9	1.41 (N20–P22)

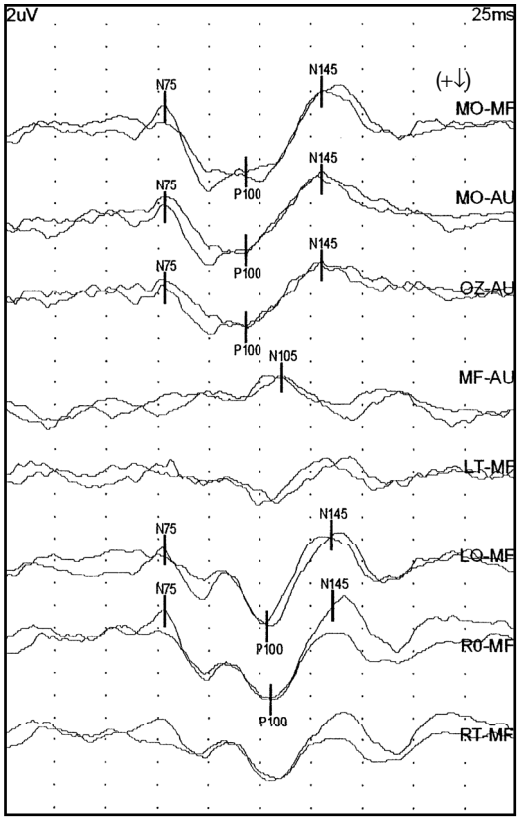
Interpeak Latencies	
Waveforms	**Latency (ms)**
EP–N20	10.9
EP–P13	5.1
P13–N20	5.8

Discussion: Low amplitude of evoked potential waveforms is seldom considered an abnormal finding unless latencies are also prolonged. Many patient-related factors (i.e., sleep), technical factors, and pathology can cause an amplitude reduction. In this median nerve SEP example, the N20 (and EP) waveform has a lower amplitude after stimulation of the left median nerve (A) compared to the right median nerve (B). Despite the amplitude asymmetry, this is considered a normal study. The latency of the N20 waveform is within normal limits.

SEP, somatosensory evoked potential.

Figure 1.13 (A and B) (*continued*)

Age: 49 years
Sex: Male
Stimulation rate: 3.9/s
Filters: 1–100 Hz
Preauricular–preauricular distance: 34 cm
Scale: Amplitude = 2 μV/div; Latency = 25 ms/div



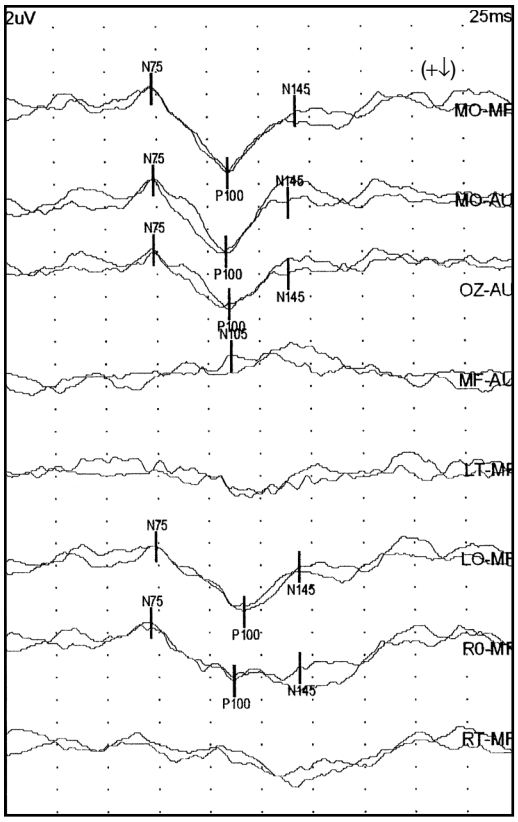
(A)
Eye: Right
Number of repetitions: 200
Visual angle: 30′
Visual acuity: 20/50
Corrective lenses: No

Absolute Latency				
Derivation	N75 (ms)	P100 (ms)	N105 (ms)	N145 (ms)
MO–MF	78.0	118.0		155.0
MO–AU	78.0	118.0		155.0
Oz–AU	78.0	118.0		155.0
MF–AU			136	
LO–MF	78.0	129.0		160.0
RO–MF	78.0	131.0		161.0

Amplitude			
Derivation	N75–P100 (μV)	P100–N145 (μV)	Mean (μV)
MO–MF	5.97	7.26	6.62
MO–AU	4.11	6.61	5.36
Oz–AU	3.61	5.72	4.67
LO–MF	6.91	8.23	7.57
RO–MF	7.93	8.39	8.16

P100 Waveform Amplitude Ratio	
Location	Ratio
OS–OD	1.02
LO–RO	1.08

Figure 1.14 (A and B) W-shaped VEP waveform. (*continued*)



(B)
Eye: Right
Number of repetitions: 200
Visual angle: 60′
Visual acuity: 20/50
Corrective lenses: No

Absolute Latency				
Derivation	N75 (ms)	P100 (ms)	N105 (ms)	N145 (ms)
MO–MF	72.5	110.0		143.0
MO–AU	73.0	109.0		139.0
Oz–AU	73.0	110.0		139.0
MF–AU			111.0	
LO–MF	73.5	117.0		144.0
RO–MF	71.0	112.0		146.0

Amplitude			
Derivation	N75–P100 (μV)	P100–N145 (μV)	Mean (μV)
MO–MF	7.68	5.62	6.65
MO–AU	6.46	4.48	5.47
Oz–AU	4.95	2.60	3.78
LO–MF	5.90	3.95	4.93
RO–MF	5.35	1.21	3.28

P100 Amplitude Ratio	
Location	Ratio
OS–OD	1.02
LO–RO	1.50

Discussion: The P100 waveform can have an abnormal morphology, and the most common such abnormality is a bi-fed peak, called a W-shaped P100 waveform. This may occur because of technical reasons, patient physiology, or visual pathway problems. In example (A), a W-shaped P100 waveform is noted after right eye stimulation. This patient also had reduced visual acuity (20/50). The PRVEP was repeated with 60′ check size (B). With the larger check size, the P100 waveform morphology improved, and there is no longer a W-shaped waveform. In this case, the W-shaped waveform occurred due to reduced visual acuity.

PRVEP, pattern reversal visual evoked potential; VEP, visual evoked potential.

Figure 1.14 (A and B) (*continued*)

technical reasons or evoked potential variability. If reduced amplitude is the only significant finding in an evoked potential study, it is seldom designated as abnormal. Most evoked potential laboratories do not have normative data for amplitude. Amplitude ratios are used more often than absolute amplitude values. They are less susceptible to technical issues and normal evoked potential variability.

Abnormal waveforms

The shape of the waveform is not used in isolation as a determinant of abnormality. This can be very variable depending on not only technical factors but also patient factors, such as alertness and anatomical variations. One type of abnormal waveform seen commonly is a bi-fed peak. This is most commonly seen with a PRVEP P100 waveform, where it is referred to as a "W-shaped" waveform (Figures 1.14A and B). Even this is frequently due to technical reasons because of how it is recorded (as discussed earlier), but sometimes it may be due to pathology.

Absence of waveforms

Complete loss of all waveforms of an evoked potential may be suggestive of severe pathology in the pathway being tested. Before this determination is made, it is important to confirm that technical problems did not cause this finding. Rechecking all components of the evoked potential machine, including the amplifiers and electrodes is very important. If all waveforms except the first are absent, pathology involving the pathway being tested is much more likely (Figure 1.15). This is because presence of the first waveform documents delivery of adequate stimulation to the neural structures.

Localization

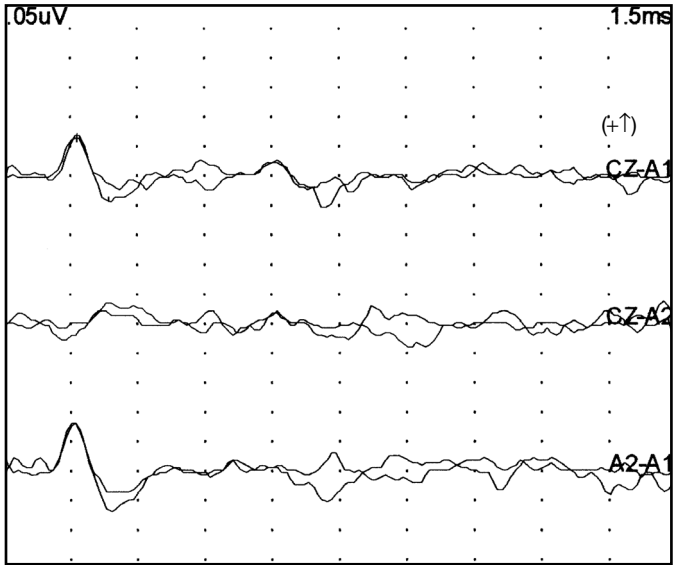
The site of abnormality can be localized in the evoked potentials by determining the pattern of abnormalities. When IPLs are prolonged, the lesion is between these two waveforms. IPL prolongations over progressively smaller regions further clarify the site of abnormality. For example, prolongation of the waves I–V IPL implies a lesion between the vestibulocochlear nerve and the inferior colliculus. In the same patient, if the wave III–V IPL is prolonged but the waves I–III IPL is not, the lesion is most likely between the superior olivary complex and inferior colliculus (Figure 1.16). Different evoked potentials can be used jointly for localization determination as well. An example of this would be if a median SEP is normal but the tibial nerve SEP shows LP–P37 IPL prolongation. The most likely site of abnormality would be above the cauda equina and below the mid cervical level.

Report

As with any other test, the report of the evoked potential study is a crucial part of the entire test. A poorly written or inaccurate report calls into question not only the technical quality of the study but also the validity of interpretation. Every report should start with a "History" section. This should briefly describe the symptoms relevant to the evoked potential study being performed. The question being asked by the referring physician should be noted. A list of medications, especially those affecting the nervous system, should be listed. It is worthwhile for the interpreting physician to be aware of the reimbursable indications for evoked potential studies in their area.

The second paragraph of the report should be the "Report" section. In this section, a brief description of the technique used to obtain the data is described. Common items mentioned in this section include which structures were stimulated, whether unilateral stimulation was used and the stimulation rate. Presence of reproducible waveforms is noted. The significant normal and abnormal parameters (mostly latencies) are listed. All latency and amplitude measurements do not need to be noted. When describing an abnormality, it is best to note the side that was stimulated to produce that abnormality. For example, instead of saying, "A right sided abnormality was noted," it is more descriptive and accurate to say, "An abnormality was noted after right sided stimulation." This takes into account that an abnormality seen with right-sided stimulation may imply a left hemispheric lesion. Toward the end of the "Report" section, it is important to describe other important measures noted in the evoked potential laboratory. This includes visual acuity for PRVEP, hearing thresholds for BAEP, and peripheral nerve conduction velocity for SEP.

Age: 5 years
Sex: Male
Stimulation rate: 11.1/s
Filters: 150–3,000 Hz
Scale: Amplitude = 0.05 µV/div; Latency = 1.5 ms/div
Side: Left
Click polarity: Alternating
Stimulation intensity: 85 dBnHL
Masking intensity: 55 dBnHL
Number of repetitions: 2,223



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
I	1.61	0.11 (I–In)
III	N/A	
V	N/A	N/A (V–Vn)
Vc	N/A	
		N/A (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	N/A
I–III	N/A
III–Vc	N/A

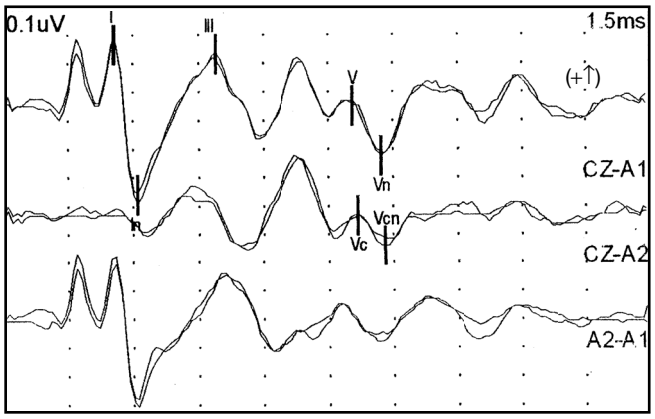
Discussion: Absence of all waveforms of an evoked potential can suggest severe pathology of the pathways involved; however, it is possible that technical problems caused these findings. When the first waveform is present and all others absent, the interpretation can be much more certain that nervous system pathology is accounting for the findings. In this example, only the cochlear microphonic is seen. This indicates that the cochlea was successfully stimulated. Absence of all other waves suggests that there is a severe lesion in the auditory pathway proximal to the cochlea.

BAEP, brainstem auditory evoked potential.

Figure 1.15 Absence of BAEP waveforms.

The next paragraph is the "Interpretation" and should state whether the test is normal or abnormal. If it is abnormal, the abnormalities are listed in order of significance. Calling a study "borderline" should be avoided. The final paragraph is the "clinical correlation." In many ways, this is the most important part of the report. In this section, the interpreting physician should determine the localization of the abnormality if present and answer the question posed by the referring physician. In the author's opinion, noting "clinical correlation required" in this section is redundant and should be avoided. Clinical correlation of the evoked potential findings as they relate to the available history is the job of the interpreting physician. Correlating the evoked potentials findings to the entire history of the patient must be done by the referring physician. This latter "clinical correlation" is implied in all tests and does not need to be explicitly restated in the "clinical correlation" section of the report. Examples of reports of normal VEP, BAEP, and SEP studies are presented (Figures 1.17A–C).

Age: 3 years
Sex: Male
Stimulation rate: 11.1/s
Filters: 150–3,000 Hz
Scale: Amplitude = 0.1 µV/div; Latency = 1.5 ms/div
Ear inserts (add 0.9 ms): Yes
Side: Left
Click polarity: Condensation
Stimulation intensity: 70 dBnHL
Masking intensity: 40 dBnHL
Number of repetitions: 2,223



Absolute Latencies		
Waveform	**Latency (ms)**	**Amplitude (µV)**
I	2.55	0.53 (I–In)
III	4.89	
V	8.04	0.18 (V–Vn)
Vc	8.16	
		0.34 (V/I ratio)

Interpeak Latencies	
Waveforms	**Latency (ms)**
I–Vc	5.61
I–III	2.34
III–Vc	3.27

Discussion: IPL prolongation helps localize the site of abnormality in evoked potentials. A prolonged IPL suggests a lesion between the generators of the waveforms between which the latency is being measured. In this example, the waves I–Vc IPL is prolonged, suggesting that the lesion is in the auditory pathway between the vestibulocochlear nerve (generator for wave I) and the inferior colliculus (generator for wave V). Further localization is possible with waves I–III and III–Vc IPLs. The waves I–III IPL is within normal limits, but the waves III–Vc IPL is prolonged. This suggests that the lesion is likely between the superior olivary complex (generator for wave III) and the inferior colliculus.

BAEP, brainstem auditory evoked potential; IPL interpeak latency.

Figure 1.16 Prolongation of IPLs of BAEP waveforms.

(A)
Visual Evoked Potential sample report

HISTORY: This is a XX-year-old patient who is undergoing a visual evoked potential study to evaluate for visual pathway dysfunction. Current medications include: XXXXXX

REPORT: Pattern reversal visual evoked responses were obtained using a XX′ check size visual arc following independent stimulation of the left and right eyes at a rate of X/s. This resulted in high signal to noise ratio with good reproducibility of the waveforms. The P100 waveform absolute latencies were normal at XX ms and XX ms following independent stimulation of left and right eyes, respectively. There was no significant side-to-side amplitude asymmetry. Parasagittal P100 waveform derivations did not show any significant latency shifts or amplitude asymmetries. The visual acuity was XX and XX of the left and right eyes, respectively.

INTERPRETATION: This is a normal visual evoked response study.

CLINICAL CORRELATION: This study does not demonstrate an abnormality in the visual pathways.

(B)
Brainstem Auditory Evoked Potential sample report

HISTORY: This is a XX-year-old patient who is undergoing a BAEP study to evaluate for brainstem dysfunction. Current medications include:

REPORT: Brainstem auditory evoked potentials were obtained following independent monaural stimulation with XX dBnHL XXXXX clicks delivered at a rate of XXX/s. All obligate waveforms were obtained with good reproducibility. The waves I–Vc IPLs were normal at XX ms and XX ms following stimulation of the left and right ears, respectively. Other IPLs and the amplitudes of the obligate waveforms were normal. A behavioral audiogram was normal.

INTERPRETATION: This is a normal BAEP study following independent stimulation of both ears.

CLINICAL CORRELATION: This study does not demonstrate abnormality in central conduction involving the brainstem auditory pathways.

(C)
Somatosensory Evoked Potential sample report

HISTORY: This is a XX-year-old patient who is undergoing an SEP study to evaluate for dorsal column dysfunction. Current medications include:

REPORT: SEPs were obtained in the upper extremities following independent stimulation of bilateral median nerves at a rate of XX/s. All obligate waveforms were obtained with good reproducibility. The waves EP–N20 IPLs were normal at XX ms and XX ms following independent stimulation of the left and right median nerves, respectively. The amplitude of the various components and other IPLs were normal. The median nerve conduction velocity was XX m/s.

SEPs were obtained in the lower extremities following independent stimulation of bilateral tibial nerves at a rate of XX/s. All obligate waveforms were obtained with good reproducibility. The waves LP–P37 IPLs were normal at XX ms and XX ms following independent stimulation of the left and right tibial nerves, respectively. The amplitude of the various components and other IPLs were normal. The tibial nerve conduction velocity was XX m/s.

INTERPRETATION: This is a normal somatosensory evoked potential study following independent stimulation of bilateral median and tibial nerves.

CLINICAL CORRELATION: There is no evidence of conduction abnormalities along the peripheral nerves stimulated, dorsal columns, or medial lemniscal pathways.

Discussion: These are sample PRVEP (A), BAEP (B), and median and tibial nerve SEP (C) reports of normal studies. All absolute and interpeak latencies do not need to be listed; only the most significant ones should be noted. Reports for abnormal studies should be appropriately amended.

BAEP, brainstem auditory evoked potential; IPL, interpeak latency; SEP, somatosensory evoked potential; VEP, visual evoked potential.

Figure 1.17 Sample VEP, BAEP, and SEP reports.

Conclusions

Clinical evoked potentials are performed in many neurophysiology laboratories, with VEP, BAEP, and SEP being the ones done most often. Since these potentials are of very low amplitude, attention to detail during acquisition is critical. Many techniques are available to enhance the waveforms. Guidelines are available to help provide consistency in acquisition and interpretation. Reports must be accurate and successfully relay the important findings of the study. Like any neurophysiologic study, evoked potentials should be repeated if additional data at a different time point would be helpful.

References

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5. Chiappa KH, Ropper AH. Evoked potentials in clinical medicine (first of two parts). *N Engl J Med.* 1982;306:1140-1150.
6. Yamada T, Kameyama S, Fuchigami Y, et al. Changes of short latency somatosensory evoked potential in sleep. *Electroencephalogr Clin Neurophysiol.* 1988;70:126-136. Figure 1.4 (A–E) Visual evoked potentials (pattern reversal)