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# An Overview about Visual and Somatosensory Evoked Potentials in Behçet Disease

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**Abstract: Background:** Behçet's Disease (BD) is a variable vessel vasculitis that involves several organs and systems, causing ulcers on the oral, genital, and intestinal mucosa, skin lesions that are most commonly in the form of papules, pustules or nodules, arthritis, uveitis, central nervous system lesions, venous and arterial thrombosis and arterial aneurysms. Evoked potentials (EPs) are electrical potentials recorded over various parts of the nervous system in response to sensory or motor stimulation. Each evoked potential has a series of waves or peaks in response to the stimulus. Clinical evoked potentials performed in a clinical laboratory most often involve stimulation of one of the sensory systems and recording the evoked potentials from peripheral nerves, spinal cord, or brain. Three types of evoked potentials are routinely used in clinical practice: visual, auditory, and somatosensory. The importance of diagnosing optic neuritis (ON) in BD is challenging because of the possibility of reversible damage in early diagnosed patients. Otherwise, the prognosis is poor with permanent blindness. Visual Eps (VEP) may be used in BD to detect ON and sub clinical optic neuritis in patients with neurological involvement. The neurological symptoms of BD may have a relapsing and remitting course with multifocal involvement of the nervous system. Chronic CNS involvement with permanent deficits is not rare IN BD. Somatosensory Eps (SSEP) studies were valuable in monitoring BD activity or therapeutic response and disclosing subclinical CNS involvement.

**Keywords:** *Evoked Potentials, Behçet Disease.*

## Introduction

Behçet's Disease (BD) is a variable vessel vasculitis that involves several organs and systems, causing ulcers on the oral, genital, and intestinal mucosa, skin lesions that are most commonly in the form of papules, pustules or nodules, arthritis, uveitis, central nervous system lesions, venous and arterial thrombosis and arterial aneurysms. Behçet disease, a chronic recurrent systemic inflammatory vascular disease, that can affect blood vessels of any type and size. The disease can present with variable clinical manifestations and the most commonly involved systems are oral, ocular, cutaneous and urogenital **(1)**.

## Evoked Potentials and Behçet Disease

**E**voked potentials (EPs) are electrical potentials recorded over various parts of the nervous system in response to sensory or motor stimulation. To adequately visualize and measure these responses, evoked potentials are usually averaged and amplified. Each evoked potential has a series of waves or peaks in response to the stimulus. Clinical evoked potentials performed in a clinical laboratory most often involve stimulation of one of the sensory systems and recording the evoked potentials from peripheral nerves, spinal cord, or brain **(2).**
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 pattern reversal VEP (PRVEP). Auditory evoked potentials (AEPs) are obtained with an auditory stimulus, most often a broadband click. Somatosensory evoked potentials (SSEPs) are obtained with electrical stimulation of peripheral nerves. Most often large mixed nerves are stimulated to obtain SSEP. In the upper extremity, median and ulnar nerves are used most often, and in the lower extremities tibial and peroneal nerves are used **(2).**

**Visual Evoked Potentials:**
VEPs are an electrophysiological examination whose findings objectively reflect the functional integrity of the whole visual pathway from the photoreceptors to the visual area in the occipital cortex **(3).**
VEPs are extracted from the ongoing EEG background activity by signal averaging and recorded from the scalp electrodes placed over the posterior head regions. Three standard stimulus protocols are defined for recording VEP, Pattern-reversal VEP, Pattern onset/offset VEP and Flash VEP. The pattern-reversal VEPs (PRVEPs) test is the standard and ideal modality for most clinical uses as it is less variable in timing and waveform than other VEP modalities **(4).**

**1- Stimulation:**

In full field PRVEP stimulation high-contrast, black and-white checkerboards consisting of squares with equal sides whose corners meet are used. The stimuli are generated on a screen, with the viewing distance about 50-100 cm. All checks are square, and equal number of light and dark checks, a fixation point position in a corner of the four checks located at the center of the field with a mean photopic luminance of about 50 cd m-2. The contrast between black and white squares is high. The black and white checks change phase (reverse) abruptly with no overall change in the luminance of the screen. The reversal rate is of 2.0 reversals per second (rps) (corresponds to 1.0 Hz, as a full cycle includes two reversals). Amplification systems electrically isolated from the patient complied with current safety standards for medical recording systems. The recording frequency band of bandpass amplifiers include the range from 1 to 100 Hz **(5).**
In contrast to the full-field stimulation that evaluates essentially the pre-chiasmal visual pathways, the hemifield stimulation can help detect abnormalities in the optic chiasm and post-chiasmal pathways. Hemifield stimulation, is challenging, time-consuming, and tiring for the patient to maintain focusing on a hemifield checkerboard pattern, the responses are low in amplitude, there is much more intra- and interindividual variability, the responses are different and complex **(6).**

**2- Recording:**

- Recording channels

Skin electrodes sintered silver–silver chloride. The skin is prepared by cleaning using a gel used to ensure good, stable electrical connection. The electrode–skin contact impedances below 5 kΩ to reduce electrical interference. The scalp electrodes placed relative to bony landmarks, in proportion to the size of the head, according to the International 10/20 system of EEG recording**.** The anterior/posterior midline measurements are based on the distance between the nasion and the inion over the vertex. For single channel recording the active electrode is placed on the occipital scalp over the visual cortex at Oz with the reference electrode at frontal midline Fz. A separate electrode is attached and connected to the ground. Commonly used ground electrode positions include the forehead, vertex, mastoid, earlobe **(5).**
Multi-channel VEP recording is not required for a basic standard clinical VEP. However, assessment of the chiasmal and post-chiasmal visual pathway dysfunction requires multi-channel recording for accurate

diagnosis. With dysfunction at, or posterior to optic chiasm there is an asymmetrical distribution of the VEP over the posterior scalp. A minimum of additional two channels is needed to detect lateral asymmetries so three active electrodes; third midline active electrode at Oz, two lateral occipital electrodes O1 and O2 (placed right and left lateral to Oz) and all three active electrodes referenced to Fz **(5).**

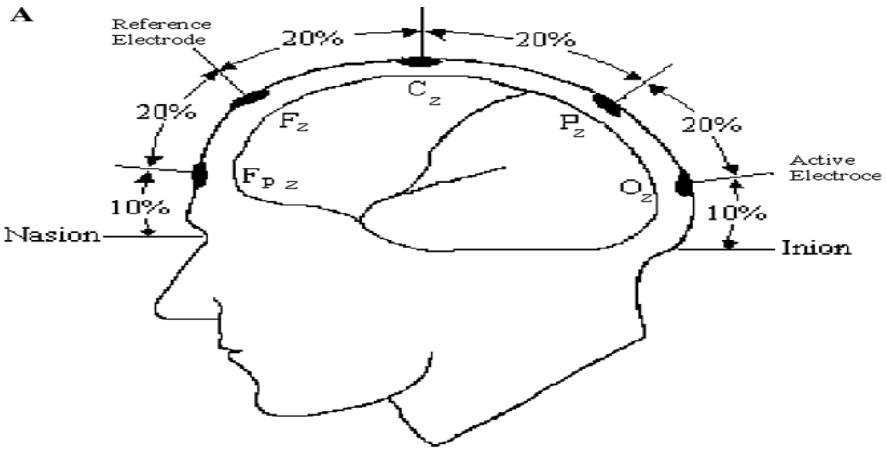


**Figure 1: Location of active and reference electrodes for standard PREVP responses. The active electrode is located along the midline at Oz. The reference electrode is located at location Fz (5).**
Oz: Occipital midline, Fz: Frontal midline, Cz: Central midline, Pz: Parietal midline, FPz: Frontopolar midline.

- **Wave Form:**

A normal VEP response to a pattern-reversal stimulus is a positive peak that occurs at a mean latency of 100 ms. There are three separate phases in the VEP waveform, named according to their latency and polarity positive (P) or negative (N): an initial negative deflection (N75), a prominent positive deflection (P100), and a later negative deflection (N145) **(7).**

The exact generator of the PRVEP has not been firmly established. There is no evidence that any of the PRVEP components are due to excitatory activities of the optic nerve, optic chiasm, optic tract, or the lateral geniculate bodies. Most of the N75 and P100 components are generated in the visual cortex. The N75 component probably represents activation of the primary visual cortex and the subsequent P100 is due to activation of the peristriate or the visual association cortex of the parieto occipital brain **(6).**

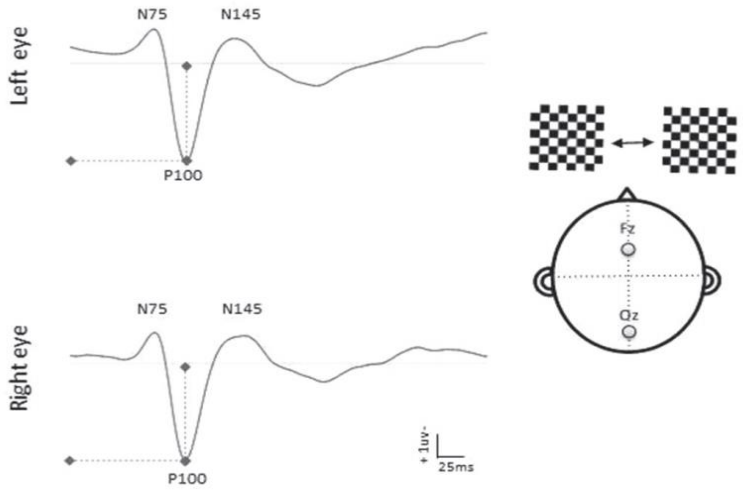


**Figure 2:** Normal PRVEP wave form (full field stimulation) **(8).**

**3- Interpretation and Criteria of Abnormality:**

The P100 latency is the single most useful measure to detect abnormalities in the visual pathways being least variable and most sensitive parameter **(9)**.

Subject-related factors like age, gender, visual acuity, severe miosis and different pupil size may affect the amplitude but may have minimal or no effect on latency, with the exception of age, where the major positivity occurs at 180 ms at 2nd month then maturation progresses slowly until age of 5 years. P100 latency is stable from about age 5 years to 60 years, the mean peak time of the P100 only slows about one millisecond per decade from 5 years old until 60 years **(7).**

If the visual acuity is 20/200 or better and there is no decrease in the retinal illumination, there is little effect on the PRVEPs with large check size. With severe refractive error and visual acuity <20/200, the PRVEP may be affected resulting in a significant decrease of the amplitude of P100, but with minimal change in the latency. If the checkerboard pattern produces a sharp image on the retina, a well-resolved PRVEP will result **(6).**

Criteria for abnormalities of PRVEP include total absence of PRVEPs, P100 latency beyond mean + 3 SD, interocular P100 latency difference of at least 10 msec and interocular amplitude ratio of P100 over 2 **(10).**

With monocular full-field stimulation, if P100 abnormality occurs only with stimulation of one eye, the dysfunction is anterior to the optic chiasm on that side. This may be due to lesions involving the optic nerve, retina, or other intraocular structures such as cornea, lens, etc**.** Once the intraocular pathology has been excluded by appropriate clinical and ophthalmological examination, monocular prolongation of the latency of the P100 is the most reliable sign of an ipsilateral optic nerve lesion. summarizes the clinical significance of major PRVEP abnormalities **(6).**

**Table 1:** Full-field PRVEPs abnormalities and their significance in lesion localizing **(6).**

| **PRVEP abnormalities** | **Interpretation** |
|---|---|
| 1. P100 latency prolongation for one eye stimulation | Pre-chiasmal dysfunction |
| 2. Interocular P100 latency difference of 10 msec | Pre-chiasmal dysfunction on the side of the prolonged latency |
| 3. Decreased P100 amplitude for one eye stimulation | Pre-chiasmal dysfunction |
| 4. Prolonged latencies of P100 for both eyes | Bilateral visual pathway dysfunction, without anterior-posterior localization |

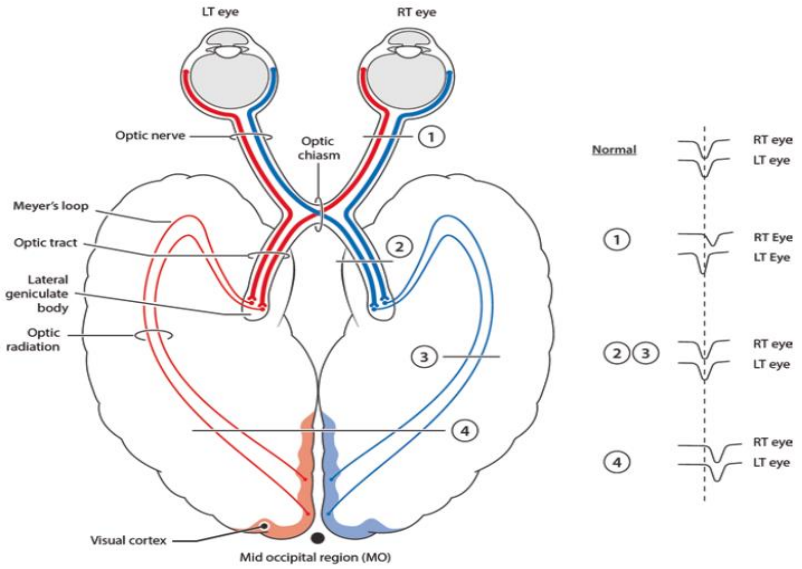


**Figure 3: The visual pathway and PRVEP abnormalities (6).**

- (1): Pre-chiasmal lesions produce ipsilateral abnormalities of P100.
- (2 and (3): unilateral post-chiasmal lesions, full-field PRVEPs remain normal.
- (4) Bilateral post-chiasmal conduction defects produce full-field PRVEP abnormalities on both right and left eye stimulations.

**4- Clinical Application of Visual Evoked Potentials:**

VEPs are utilized in various clinical situations such as: detection of an optic nerve lesion or subclinical involvement in patients with multiple sclerosis (MS), detection of subclinical visual pathways involvement in patients with neurofibromatosis or heredofamilial ataxias or who had an exposure to certain antibiotics or toxins, confirmation of present or past lesions in patients with visual symptoms (e.g., optic nerve tumor and optic neuropathies), evaluation of visual impairment suspected to be due to conversion disorder or malingering and assessment of visual function in children who are suspected to have poor visual acuity or blindness **(6).**

The pathological conditions producing PRVEP abnormalities are diverse. In focal segmental demyelination as occurs with MS, VEP abnormalities are primarily of prolonged latencies with preserved amplitude. A demyelinating optic neuropathy associated with multiple sclerosis commonly produces ipsilateral increase in P100 latencies with little or no change in the amplitude, while compressive, ischemic, or degenerative processes involving optic nerves usually produce a conduction block, which results in a decreased amplitude of PRVEPs with variable effect on latency **(11)**.

In cases of optic neuritis, the VEP examination is valuable for both the diagnosis and the monitoring of the disease. In multiple sclerosis, it can also diagnose subclinical optic nerve involvement, even if optic neuritis is not obvious. Furthermore, VEPs are recorded as abnormal in maculopathy, in ocular media opacities and in amblyopia **(3).**

VEPs testing can be used to predict the extent of recovery after optic neuritis (ON) and capture disabling effects of clinical and subclinical demyelination events in the afferent visual pathway**.** VEPs can help to monitor and detect deterioration and improvement in MS patients **(12).**

ON is a rare manifestation in BD but underestimated condition, probably due to associated uveitis. The importance of diagnosing ON is challenging because of the possibility of reversible damage in early diagnosed patients. Otherwise, the prognosis is poor with permanent blindness. VEP may be used in BD to detect ON and sub clinical optic neuritis in patients with neurological involvement **(13).**

Ocular pathology in BD is also well recognized to mirror CNS pathology and there may be an association between ischemic demyelination of the optic nerve and the CNS **(14).**

**Somatosensory Evoked Potentials (SSEP):**

The SSEP responses are generated along large fiber sensory pathways, primarily fibers carrying proprioceptive sense, but also touch and vibration. A traveling potential created by electrical stimulation passes along the pathway and SSEP responses are recorded from locations where the signal changes direction or reaches a subsequent generator. All changes in direction of the traveling signal are reflected by peaks that are predictable, relatively steady, and reproducible. These individual peaks are named based on their latency after the stimulus and by their polarity **(15).** The recorded potentials are such that upward deflections reflect negativity (labeled N) of the potential at the active electrode and downward deflections reflect positivity (P). The number following N or P refers to the average latency at which this potential is recorded in normal subjects. SSEPs are considered short-latency potentials, occurring in the first 30ms after stimulation of upper-limb mixed nerves and within 50ms after stimulation of lower-limb mixed nerves. By comparison, long-latency SEP waveforms occur after 100ms following stimulation, and mid-latency SEP potentials occur between short- and long-latency values **(6),** Such as P45-N60 over the contralateral upper limb area of somatosensory cortex of, N30-P65-N70 over the frontal cortex and N60, P100 over contralateral area of lower limb area of the somatosensory cortex. Although the amplitude of short-latency SSEP is smaller than the medium- or long-latency SSEP, the stable nature of short-latency SSEP makes it more suitable for neurological diagnostic tests **(16).**

1. **Stimulation:**

The electrical stimulation to the peripheral nerve is technically simple and yields distinct responses along the sensory pathway. Both mixed (motor and sensory) and pure sensory nerve stimulations will evoke an SSEP of similar waveform, but the response is generally larger with mixed than with pure sensory nerve stimulation. For this reason, mixed nerve stimulations are more commonly used for clinical diagnostic tests. Stimulus electrodes are applied to the skin overlying the nerve to be stimulated **(6).**

SSEPs are usually evoked by bipolar transcutaneous electrical stimulation applied on the skin over the selected nerve. Monophasic square-wave electrical pulses of 0.1– 0.2 ms should be delivered, preferably by a constant current stimulator. In routine recording, stimulus parameters include a stimulus intensity able to produce a clear but tolerable sensation and produce a minimal muscle twitch. The stimulation rate should be 3–5 Hz and as far as possible, the same intensity should be kept for both sides. The cathode should be proximal to reduce the likelihood of anodal block. A ground electrode is placed on the stimulated limb between the stimulation site and the recording electrodes to minimize stimulus artifact **(17).**

For upper extremity SSEP, the median or ulnar nerve is stimulated. The most used electrode is a bar electrode with two imbedded electrodes, one acting as a cathode and the other as an anode. Median nerve is stimulated with the anode is placed 2 to 3 cm proximal to the distal crease of the wrist, and the cathode is about 2 cm proximal to the anode. For lower extremity SSEP, the tibial nerve is commonly used, and rarely peroneal. Tibial nerve is stimulated at the medial aspect of the ankle, along the medial malleolus. These are mixed nerves containing both motor and sensory nerve fibers **(14).**

2. **Recording:**

- **Recording Principles:**

Different from electroencephalography (EEG) which reflects the brain's spontaneous electrical activity over a short period of time, SSEPs are not recorded continuously to spontaneous stimuli but are time locked to a stimulus with a pre trigger. SSEP peak amplitudes are traditionally in the under 10μV range **(18).**

A combination of bipolar and referential recording montages\channels (montages are specific arrangement of channels, channel is a pair of electrodes) is used for SSEP recordings. In a bipolar montage, both recording electrodes are electrically active. In a referential montage, the inactive electrode should be placed far enough from the generator to be electrically silent and is usually noncephalic (e.g., on the opposite mastoid, shoulder,

arm, hand, or knee). The larger the distance between the electrodes, the higher the likelihood of introducing unwanted noise to the recording, especially muscle artifact that may obscure smaller potentials **(13).**

The generated SSEPs can be divided into near-field and far-field components. Near-field potential responses are recorded from electrodes close to the generator site, such as the peripheral nerve, spinal cord, or cerebral cortex, and have a narrow recording distribution. These potentials are characteristically of negative polarity, of relatively large amplitude, and sensitive to electrode placement, their amplitude decreases as the recording electrode is moved away from the generator source. Cortical near-field potentials are best recorded with a bipolar cephalic derivation. **(2).**

Far-field potential waveforms are generated distant from the recording electrodes and have a broad distribution. These potentials are usually of small amplitude, are best seen in referential montages, they can be recorded over a wide area of scalp with equal ease and amplitude. Evoked potentials recorded from brainstem structures are examples of far-field potentials, the advantage of far-field recording is the ability to obtain the information along the whole sensory pathway from a single recording montage encompassing multiple generators and recording sites, disadvantages include the small amplitude of the responses and electrical noise introduced from muscle artifact due to long interelectrode distances creating potential error **(13).**

To most effectively, and efficiently record cortical SSEPs signals, it is recommended that one centimeter surface recording EEG electrodes should be placed as per the 10-20 international EEG system **(19).**

Skin at the scalp EEG electrodes should have less than 5 Kohms impedance. The number of waveforms that need to be averaged is between 500 and 2000 stimuli presentations, in order to clearly differentiate the signal from noise **(16).** Clinical Neurophysiology guidelines recommend a filtering bandwidth with a high pass of 3 Hz and low pass of over 2000 Hz to isolate reproducible waves from background noise **(15).**

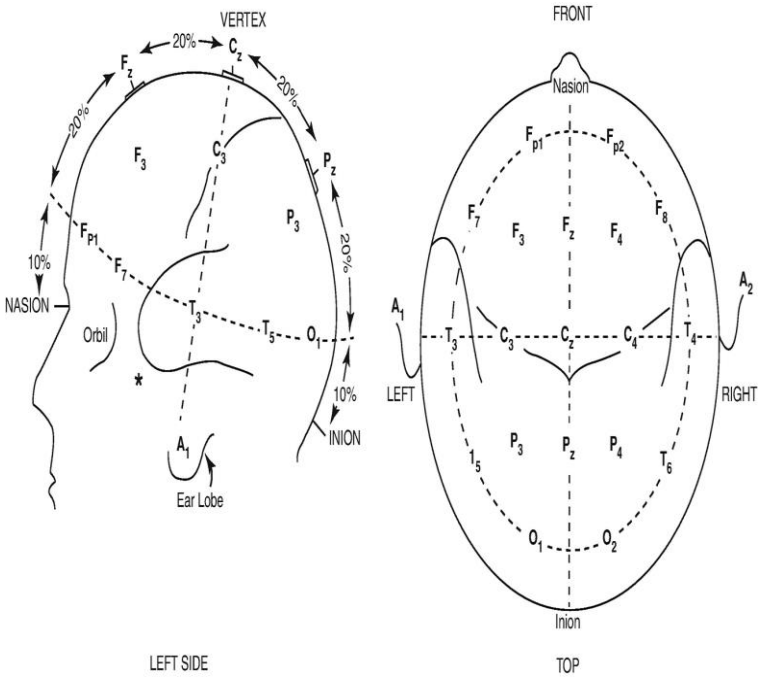


**Figure 4:** The international 10–20 system is used for cortical electrode placement **(20).**

- These electrodes include: Fronto-polar (Fp), Frontal (F), Central (C), Temporal (T), Parietal (P), Occipital (O). Auricular or earlobe (A).
- Odd numbers refer to the left-sided electrodes and even numbers to the right. For example, F3 is the left frontal electrode, and F4 is the right frontal.

- The letter "z" designates midline. For example, Cz is midline central.

- **Recording Electrodes Location and Recording Montages:**

There has been a marked variability in the literature regarding the location of the electrodes (especially reference electrodes) and the montages used for recording SSEPs, each recording channel is designated to record certain generated potential of the SSEP **(13).**

The generators of SSEP potentials are derived from peripheral nerves (PN) and central structures including spinal cord, brain stem and sensory cortex, which generate different types of recorded potentials **(6).**

**A. Upper limb SSEP recording channels and generated waves:**

**Table 2**: Different electrode location and montages for SSEP recording **(13).**

| **A-Upper limb** | | |
|---|---|---|
| **Channels** | **Active electrode** | **Reference electrode** |
| **Peripheral channel 1:** Record peripheral N9 potential. | **Epi** (Erb's point ipsilateral). placed within the angle formed by the posterior border of the clavicular head of the sternomastoid muscle and the clavicle, 2–3 cm above the clavicle (Erb's point). | **EPc** (Erb's point contralateral) **or Fz** (Frontal midline). |
| **Cervical channel 2:** Record cervical N13 potential. | **C5s** ($5^{th}$ cervical spine) **or C7s** ($7^{th}$ cervical spine). | **Fz** **or Epc** **or AC** (Anterior neck). |
| **Cortical channel 3:** Record sub cortical P14, N18 potentials. | **Cpi** (Centroparietal ipsilateral to stimulation site) Centro-parietal scalp electrodes (CP) are placed on the left side between C3 and P3 and on the right side between C4 and P4 of the 10–20 electrode placement system. Then renamed as CPi (Centroparietal ipsilateral) and CPc (Centroparietal contralateral) according to the side of stimulation. | **Epc** (Contralateral Erb's point). |
| **Cortical channel 4:** Record cortical N20 potential. | **Cpc** (Centroparietal contralateral to stimulation site). | **Fz** **or Cpi.** |

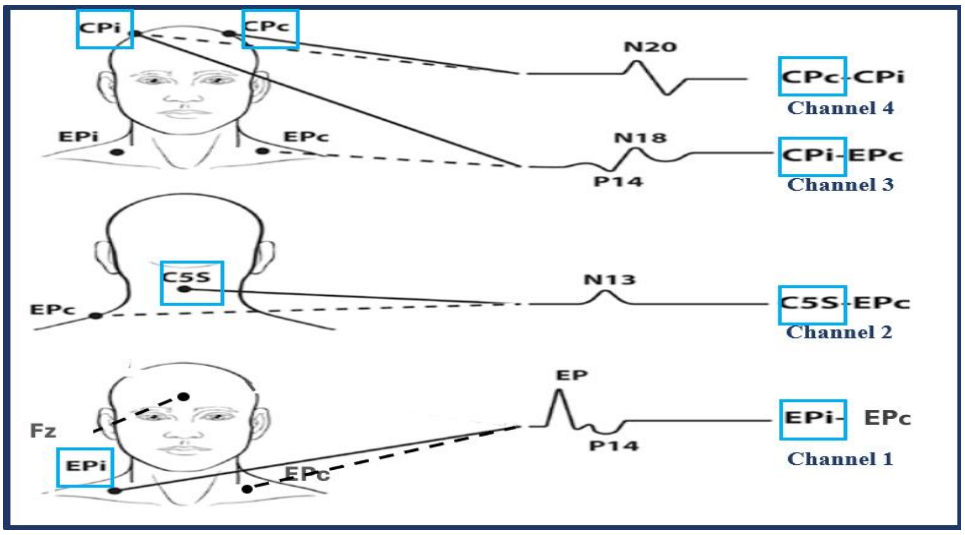


**Figure 5: Recording channels for upper limb SSEP and wave forms (6).**

Blue boxes show the main active electrodes. Reference electrodes vary across different literature.

Chanel 1: active electrode EPI, reference electrode: EPc (or Fz).

Chanel 2: active electrode C5s, reference electrode: EPc (or Fz, Ac).

Chanel 3: active electrode Cpi, reference electrode: EPc.

Chanel 4: active electrode CPc, reference electrode: Cpi (or Fz).

EPI: Erb's point ipsilateral, EPc: Erb's point contralateral, C5s:5$^{th}$ cervical spine, Cpi: cortico-parietal ipsilateral, Cpc: cortico-parietal contra lateral, Fz: frontal midline, AC: anterior neck.

**Upper Limb SSEP Generated wave forms:**

- **Erb's point potential (N9):**

This potential is recorded over the ipsilateral point Erb's and represents a near-field and propagated compound nerve action potentials of the median nerve as they arrive at the brachial plexus. When evoked by median nerve stimulation, it represents orthodromic activity in median sensory fibers that enters the spinal cord via the dorsal C6–C7 cervical roots in addition to the antidromic median motor fiber impulses via C8–T1 cervical roots. Erb's point potential is usually a biphasic (positive-negative) or triphasic (positive-negative-positive) potential. The peak of the negativity occurs at a mean latency around 9–10 msec after the stimulation of the median nerve at the wrist, hence it is designated as N9 **(21).**

- **Cervical potential (N13):**

Recording over the posterior aspect of the cervical spine demonstrates a stationary non-propagated near field potential (N13) over the cervical C5or C7 spine process reflects excitatory postsynaptic potentials in the dorsal horn grey matter of the cervical cord at the root entry zone. The amplitude of this potential is highest over the mid cervical spine, but it is recordable at higher and lower cervical regions with lower amplitude, but with fixed latency. Its mean latency is 13 msec from the time of median nerve stimulation at the wrist **(13).**

- **Subcortical potentials (P14 and N18):**

Both P14 and N18 are considered to arise from activation of somatosensory structures in the brainstem, P14 is low in amplitude and appears either as a single positive component or with a bifid waveform. It is widely distributed over the scalp, hence, recordable only by using scalp-to-non-cephalic derivation (e.g., CPi-Epc). P14 most probably reflects activity in the caudal medial meniscus. N18 also is a subcortical far-field potential recorded referentially from scalp electrodes and probably reflects activity in the caudal medial lemniscus, Earlier studies thought it arose from the thalamus **(6).** Sub cortical components are important when using SSEP in intensive care units for evaluation of brain stem and cortical function **(15).**

- **Somatosensory cortical potential (N20):**

This is a near field, cortical potential with a broad V- or W-shaped response, the earliest component of which has a mean latency of 20 msec. This reflects the excitatory postsynaptic potentials generated in the primary somatosensory cortical, neurons of hand area in response to the afferent thalamocortical volley **(22).**

**B. Lower limb SSEP recording channels and generated waves:**

**Table 3**: Different electrode location and montages for SSEP recording **(13).**

| **B-Lower limb** | | |
|---|---|---|
| **Channels** | **Active electrode** | **Reference electrode** |
| **Peripheral channel 1:** Record peripheral N8 potential. | **PF** (Popliteal fossa) 4-6 cm above mid popliteal crease. | **Knee** on the medial femoral condyle or 3cm above active electrode. |
| **Lumbar channel 2:** Record lumbar N22 potential. | **T12s** (12th thoracic vertebrae) **or L1** (1st lumbar) | **IC** (Iliac crest) contralateral side. **or L3** (3rd lumbar) **or over umbilicus** |
| **Cortical channel 3:** Record sub cortical P31, N34 potential. | **Fpz** (Fronto polar midline) | **C5s** **or C7s** |
| **Cortical channel 4:** Record cortical P37 potential. | **Cpz** (Centroparietal midline) - Centro-parietal midline electrode, (CPz) located midway between Cz and Pz of the 10–20 electrode placement system. - Patients where CPz-FPz derivation does not adequately record P37 potential an additional derivation slightly off the midline of CPi-FPz is recommended. | **Fz** **or Fpz** |

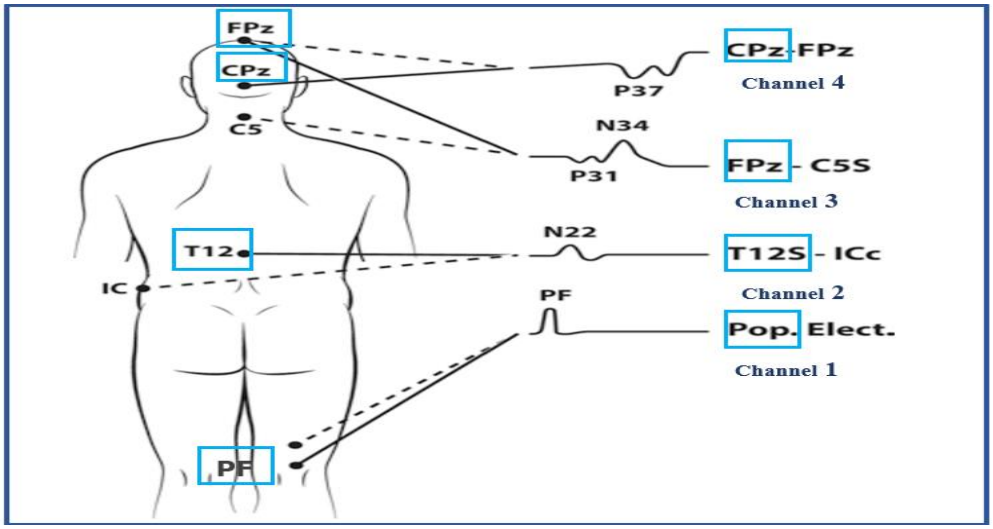


**Figure 6: Recording channels for lower limb SSEP and wave forms (Markand & Omkar, 2020).**
**Blue boxes show the main active electrodes. Reference electrodes vary across different literature.**
Chanel 1: active electrode: PF, reference electrode: 5cm above knee (or medial femoral condyle).
Chanel 2: active electrode: T12, reference electrode: IC contralateral (or L3, umbilicus).

Chanel 3: active electrode: FPz, reference electrode: C5S (or C7S).
Chanel 4: active electrode Cpz, reference electrode: Fpz (or Fz).
PF: popliteal fossa, T12: 12$^{th}$ thoracic spine, C5s:5$^{th}$ cervical spine, Cpz: cortico-parietal midline, Fpz: frontopolar midline, Fz: frontal midline, IC: iliac crest.

**Lower Limb SSEP generated wave forms:**

- **Popliteal potential (N8):**

In the peripheral channel, over the popliteal fossa a traveling propagated compound nerve action potential is recorded, which has a classic triphasic waveform. The mean latency of the negative peak is usually 7–8 msec, hence, the designation N8 for this potential. The presence of a robust popliteal potential establishes a satisfactory stimulation of the posterior tibial nerve, and the latency provides a sensorimotor conduction time between the ankle and the popliteal fossa. **(16).**

- **Lumbar potential (N22):**

The second channel records the lumbar potential which is usually a monophasic or a biphasic potential whose negative peak occurs at a mean latency of 22 msec, although it is widely distributed over the lower thoracic and upper lumbar spine, it is a stationary near-field potential which decreases in amplitude above and below the T12/L1 spinal level, but the latency remains fixed. Recording from closely placed electrodes ("bipolar" recording) over the thoracolumbar spine may attenuate the potential significantly because of the in-phase cancellation. A reference electrode over the opposite iliac crest is another way to record N22 potential. Posterior tibial N22 is analogous to the median N13 and reflects excitatory postsynaptic potentials due to activation of the dorsal gray of the lumbar cord **(13).**

- **Subcortical potentials (P31, N34):**

Similar to P14/N18 of the median, it is a referential recording using scalp-to-non-cephalic reference, demonstrates a small positive component P31, followed by a more prominent negative component N34. These are far-field potentials with generator sources in the sensory structures located in the brainstem. P31 and N34 are probably analogous to P14 and N18 of the median SEPs **(6).**

- **Cortical potential (P37):**

A "W"-shaped waveform recorded from a "bipolar" scalp-to-scalp derivation by the fourth cortical channel over Cz, it is a near-field cortical potential with initial positivity, which has the mean latency of 37–38 msec (P37), represents the activation of the cortical somatosensory receiving areas for the lower extremities. It is usually maximum at the midline centro-parietal (CPz) electrode, but at times the area of maximum amplitude may be shifted to the lateral parasagittal region ipsilateral to the stimulated lower extremities, this "paradoxical" lateralization of P37 to ipsilateral parasagittal scalp is explained by the deeper location of the activated cortical zone along the interhemispheric fissure with a resultant net direction to the opposite side **(23).**

**3. Interpretation and Criteria of Abnormalities:**

The clinical interpretation of SSEP depends on the anatomo-functional relationship of the generators of the different waves**.** The absence of a component suggests that the path is compromised at the previous segment or at the level of its generator. The presence of an expected component, but with prolonged latency, suggests the existence of a compromised myelin pathway **(24).**

Abnormal SSEP may include absence of certain potentials, prolongation of peak latencies or prolongation of inter peak latencies (IPL), that may aid in approximately localizing the site neurologic dysfunction**. (6). Table 4 and 5** shows abnormal SSEP finding of median and tibial nerve stimulation and their interpretation**.**

Absence of waveform is considered an amplitude abnormality. This may be due to either the dysfunction of the generator itself or failure of the generator to receive the afferent input. Subcortical components in general and cervical as well as lumbar components are often poorly resolved in an awake patient who is tense and unable to relax, their absence therefore cannot be taken as an abnormality. Absolute amplitude of SSEP components is of limited diagnostic significance because of marked intersubject variability. A 50% reduction in the amplitudes

on one side is often considered as a "soft" abnormality, but this is relevant only if the recording electrodes are symmetrically placed and the nerves on the two sides are optimally stimulated **(25).**

Absolute latencies and interpeak latencies (IPLS) beyond 2.5–3.0 SD from the mean for a normal population studied in a laboratory are usually considered as abnormal. Because the absolute latencies of individual components are affected by age, limb length, body temperature, and peripheral conduction time, the IPLs are considered as better parameters to assess conduction in the central somatosensory pathways **(25).**

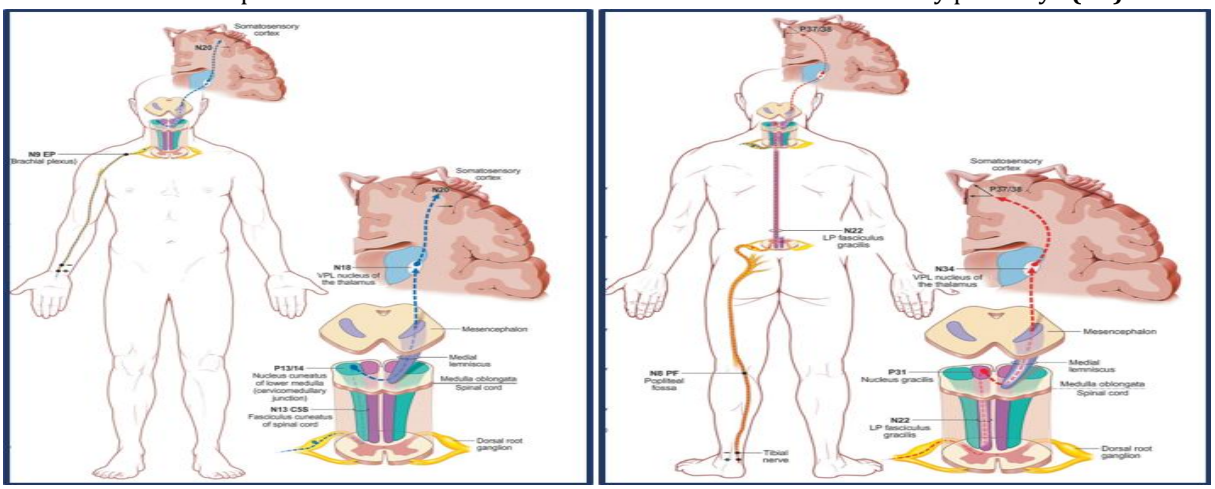


**Figure 7: Neuroanatomy pathway and corresponding SSEP wave forms of upper limb SSEP after right median nerve stimulation and lower limb SSEP after right tibial nerve stimulation (13).**

SSEP: somatosensory evoked potentials.

**Table 4:** Common median SSEP findings and their clinical interpretation for localization of a neurologic insult **(6).**

| | **Median SSEP findings** | **Interpretation** |
|---|---|---|
| 1 | N9, N13, and P14 are normal, but N20 is delayed (prolonged IPL P14-N20) | Conduction defect between foramen magnum and sensory cortex, but not involving the cortex |
| 2 | N9, N13, and P14 are recordable at normal latencies, but cortical response is absent | A dysfunction either in the sensory cortex itself or the thalamocortical projections to the sensory cortex |
| 3 | N9 and N13 are recordable at normal latencies, but P14 and N20 are absent | Conduction block in the intracranial somatosensory pathways rostral to foramen magnum |
| 4 | Normal N9 but delayed N13 or P14 (N9-P14 or N9-N13 IPL prolongation) | A conduction defect in the sensory system central to the brachial plexus and below the foramen magnum (peripheral and/or central involvement) |
| 5 | Normal N9, prolongation of both N9-N13 and N13-N20 IPLs | Conduction defect central to the brachial plexus below and above the foramen magnum |
| 6 | N9 has prolonged latency, centrally generated components (N13, N20) also prolonged, but IPLs are normal. | Conduction abnormality is peripheral as may occur with a peripheral neuropathy. |
| 7 | N9 is absent but centrally generated components recordable at normal latencies | Test is interpreted as normal; absent N9 may be technical |
| 8 | N9 is absent and N20 recordable but at a prolonged latency with delayed or absent N13 and/or P14 components | Slowing of conduction most likely peripherally (e.g., neuropathy) with or without central conduction slowing |

SSEP: somatosensory evoked potentials, IPL: inter peak latency.

**Table 5:** Common posterior tibial SSEP findings and their clinical interpretation **(6).**

| | **Posterior tibial SSEP findings** | **Interpretation** |
|---|---|---|
| 1 | N7 or N8 and N22 are recorded at normal latencies, but P37 is delayed (IPL N22-P37 prolonged) | Conduction defect in large sensory fiber system rostral to lumbar cord and below sensory cortex. |
| 2 | N7 and N22 are normal, but P37 is absent | Conduction defect is anywhere rostral to the lumbar cord including even the sensory cortex |
| 3 | N7 and/or N22 are non-recordable, but P37 is normal | Test is interpreted as normal; non-recordability of peripheral and lumbar potentials may be technical |
| 4 | N7 is of normal latency, but N22 is delayed (prolonged IPL N7-N22), but IPL N22-P37 is normal | Conduction defect is peripheral to the lumbar cord, virtually always in the peripheral nervous system |

| | | |
|---|---|---|
| 5 | N7 is at a normal latency, N22 is absent, and P37 is delayed (prolonged IPL N7-P37) | Conduction defect may be in the peripheral and/or central somatosensory pathways |
| 6 | N7 is recorded at a prolonged latency, but the IPLs N7-N22 or N7-P37 are normal | Conduction slowing is peripheral to the popliteal fossa Check for cold lower limb |

SSEP: somatosensory evoked potentials, IPL: inter peak latency.

**4. Clinical Application of Somatosensory Evoked Potentials:**

Clinical evoked potentials (EPs) allow non-invasive functional examination of the sensorimotor pathways. MRI in a clinical setting is superior in terms of anatomic accuracy and detection of underlying pathologies however, electrophysiological techniques allow non-invasive exploration, provide quantitative information on the functional status of selected functional systems, and can be repeated as often as necessary with relatively low cost. EP studies allow the detection of subclinical lesions and the prediction of long-term disability and conversion to symptomatic disease phases **(8).**

**a- Peripheral nervous system disorders:**

Generally, the SSEPs do not constitute the first line of testing if the patient is suspected having a peripheral nervous system disorder because the traditional sensory motor conduction studies, F-wave latencies, and H reflexes provide diagnostically more useful information. If the peripheral studies have been non-revealing, SSEPs may be utilized to detect a possible dysfunction of the proximal portion of the peripheral nervous system. An example is acute and chronic inflammatory demyelinating polyneuropathy, plexopathy, radiculopathy and thoracic outlet syndrome **(26).**

**b- Central nervous system (CNS) disorders:**

In the CNS disorders SSEPs find its major utility for assessing the integrity of the dorsal column-lemniscus pathways from the level of the spinal cord to its termination in the somatosensory cortex. The major clinical conditions commonly evaluated by SSEPs include brain death and coma, demyelinating disorders (e.g., multiple sclerosis, leukodystrophy), tumors of the spinal cord or brainstem, myelopathies (acute or chronic) and other miscellaneous CNS disorders (e.g., stroke, amyotrophic lateral sclerosis, ataxia, vitamin B12 deficiency) **(6).**

SSEP recording is an objective technique and is often more sensitive than the traditional neurological component of physical examination for evaluation of comatosed, anesthetized patients. Interpretation of the presence and absence of specific waveforms can be utilized to predict comatose patient prognosis **(16).**

Demyelinating diseases have been the focus of study with the evoked potentials, trying to find a neurophysiological biomarker for diagnosis, prognosis or therapeutic response. SSEP can provide important information in multiple sclerosis with cerebral or spinal cord involvement and in selected patients with suspected multiple sclerosis (MS) and uncertain MRI findings. **(22).**

The neurological symptoms of BD may have a relapsing and remitting course with multifocal involvement of the nervous system. Chronic CNS involvement with permanent deficits is not rare. In a young patient, such a neurological course may mimic MS **(27).** It was suggested that the EPs studies were valuable in monitoring BD activity or therapeutic response and disclosing subclinical CNS involvement **(28).**

Segmental cervical cord dysfunction in spondylotic cervical myelopathy has been associated with an abnormal N13. SSEP are useful also in other types of myelopathies which are secondary to compression, ischemia, trauma, inflammatory processes, demyelination, and paraneoplastic **(13),** or secondary to autoimmune disorder that may cause myelitis e.g., neuromyelitis optica, antiphospholipid antibody syndrome, neurosarcoidosis, sjögren's syndrome and rarely BD **(29).**

SSEPs can be abnormal in hereditary spastic paraparesis, primary lateral sclerosis, and amyotrophic lateral sclerosis (ALS). The exact underlying pathogenic mechanism of SSEP changes in ALS is not well understood but may represent nonmotor system involvement or motor-sensory system connectivity **(13).**

**c- Intra operative monitoring:**

Important advances have been made in recent years with intraoperative neurophysiological monitoring, where SSEP play a fundamental role, with the aim of minimize neurological damage, to identify important neural structures and thus to avoid and/or limit significant postoperative impairments. While most frequently used

on orthopedic spinal procedures like scoliosis correction, SSEPs has proven useful for warning surgeons of impending brain damage on aneurysm clipping other neurovascular interventions **(30)**

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