

REVIEW

The SSEP on the ICU: current applications and pitfalls

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Abstract

Clinical neurological evaluation of patients in the intensive care unit (ICU) is often limited. Registration of the somatosensory evoked potential (SSEP) can assist in the neurological evaluation in these patients. In this paper, we discuss the principles, applications and limitations of the SSEPs in the ICU with a focus on prognostication in comatose patients. Registration of the SSEP is a very reliable and reproducible method, if it is performed and interpreted correctly. A bilateral absent cortical SSEP response is a reliable predictor for poor neurological outcome in patients with a post-anoxic coma, but not in patients with traumatic brain injury or subarachnoid haemorrhage. During SSEP recordings, great care should be taken in improving the signal to noise ratio. Since the interpreting clinician is often not present during the actual SSEP registration itself, the role of the lab technician is crucial in obtaining reliable SSEP results. If the noise level is too high, the peripheral responses are abnormal, or the response is not reproducible in a second set of stimuli, interpretation of the SSEP cannot be done reliably.

Introduction

Neurological evaluation of patients in the intensive care unit (ICU) is often limited, and clinical neurophysiology has provided several techniques to assist in the evaluation of the central and peripheral nervous system in these conditions. Techniques include the electroencephalogram (EEG), brainstem auditory evoked potentials (BAEP) and the somatosensory evoked potential (SSEP). In this paper, we discuss the principles, applications and limitations of the SSEP. SSEPs are used in a variety of clinical settings, including the evaluation of coma, neuromonitoring in the operating theatre, and the evaluation of traumatic spinal cord injury. Here, we focus on the use of the SSEP registration in the prognostication of comatose patients in the ICU.

SSEP: Principles

The somatosensory evoked potential is a small (< 10-50 μ V) electrical signal, that can be recorded noninvasively from the skull,

after giving a set of electrical stimuli to one of the peripheral nerves. Measurement of the SSEP evaluates the complete pathway from the peripheral sensory nervous system to the sensory cortex, which runs via the dorsal column lemniscal pathway via the spinal cord, brainstem and thalamus^{1,2}.

The dorsal column-lemniscal pathway consists of four neuronal populations. The cell bodies of the first-order neurons are situated in the dorsal root ganglia, the trigeminal ganglion, the midbrain trigeminal nucleus, and the vagal ganglion nodosum. The second-order neuron lies in the dorsal column nuclei (the cuneate nucleus and the gracile nucleus). Axons of these second neurons cross the midline and project to the ventroposterior nuclei of the thalamus (third-order neuron). From there the pathway projects into the network of somatosensory cortex areas (fourth-order neurons), which include primary and secondary somatosensory cortex, posterior parietal cortex, posterior and mid-insula, and mid-cingulate cortex¹. *Figure 1* shows the anatomical connections evaluated by the median nerve SSEP.

SSEPs are usually evoked by bipolar transcutaneous electrical stimulation applied on the skin over the selected nerve, and registered with disk-electrodes along the tract. For example, in SSEP recordings of the median nerve registration electrodes can be placed at the elbow, Erb's point, cervical, parietal and frontal cortex. The cortical response can only be interpreted reliably, when the peripheral responses are present.

In the nomenclature of SSEP waveforms, N or P followed by an integer (e.g. N20) are used to indicate the polarity and the nominal post-stimulus latency (in ms) of the recorded wave in the healthy population¹. The earliest cortical potential is the N20, which is generated in the primary somatosensory cortex, where thalamocortical cells make synaptic connections with the superficial and deep pyramidal cell layers^{3,4}. In comparison to the later cortical responses, the N20 is the most robust, and is the latest waveform to disappear during increasing levels of encephalopathy. Furthermore, the N20 is relatively independent to the level of sedation¹. As the

later cortical waveforms (P45, N60 and P/N100) are less reliable and more susceptible to changes by sedation, the N20 is used in all prognostic clinical routines.

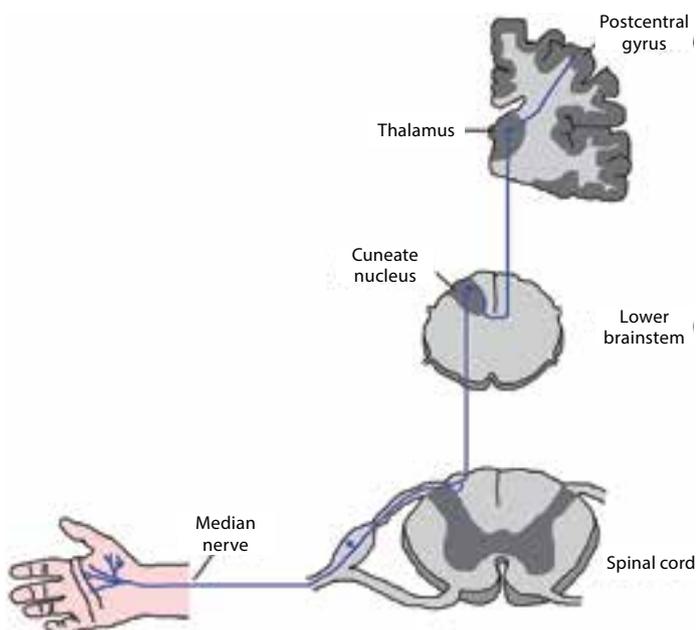
The N20 SSEP in Prognostication

Postanoxic Coma

Bilateral absence of short latency (N20) SSEP response has been identified as the most powerful predictor of poor outcome in patients who are unconscious after circulatory arrest¹. In patients not treated with hypothermia, bilateral absence of cortical N20 responses 24 hours or more after the ischemic event is a reliable predictor for a poor neurological outcome^{5,6,7}. A systematic review of Robinson showed a false positive rate (FPR) of 0%⁶, while a meta analysis of Wijdicks et al. found a 0.7% false positive rate for bilateral absent N20 responses in those patients⁷.

In patients treated with therapeutic hypothermia, absence of the N20 also indicates a poor prognosis. In two large prospective studies, including 228 patients, the median nerve SSEP was found to be a reliable tool to predict a poor outcome after rewarming with an FPR of 0%^{8,9}. However, a retrospective study of Leithner in 122 available SSEPs revealed one patient treated with therapeutic hypothermia after cardiac arrest with bilateral absent N20 responses at day 3 with good neurological outcome¹⁰. This SSEP was measured on day 3 under sedation with midazolam and fentanyl in a patient with alcoholic polyneuropathy. Despite this single case, pooled analysis of these three recent studies^{8,9,10} on cardiac arrest patients after hypothermia still give very low FPRs of 0.9%, indicating that bilateral absence of the N20 should still be viewed as a reliable predictor for poor outcome in patients treated with hypothermia.

Figure 1. The anatomical connections evaluated by the median nerve SSEP



Recent studies show that already during the period of hypothermia the SSEP is a reliable tool to predict a poor outcome^{9,11,12,13}. A pooled analysis of these four prospective studies (424 patients), shows an FPR of 1.5% with a sensitivity of 28%. The FPR of 1.5% results from three patients with good neurological outcome and bilateral absent N20 responses during hypothermia, who were reported in the study of Bouwes et al⁹. However, in a post hoc assessment of these SSEP registrations it was concluded that these three SSEP recordings were undeterminable because there was too much noise in the registration⁹. Correction of these results led to an FPR of 0%.

Unfortunately, preservation of the N20 does not imply a favourable outcome in patients after cardiac arrest. In fact, only a small proportion of patients with a poor outcome after resuscitation have negative SSEP responses resulting in a low sensitivity. This low sensitivity of the SSEP is also reflected in the large variability of EEG patterns that can be observed in patients with a preserved N20, including status epilepticus or even electro-cerebral silence⁴. As pyramidal cell synaptic function is mainly reflected by the EEG, while SSEP mainly evaluates the thalamocortical synaptic function, a possible explanation is selective hypoxic damage to the cortical pyramidal cells' synaptic function, with preserved thalamocortical synapses⁴.

Traumatic Brain Injury

In patients with severe traumatic brain injury (TBI), the results available on the reliability of SSEP to predict outcome have been contradictory. Sleigh et al. showed in a prospective blinded cohort study including 105 patients that the median nerve SSEP is a reliable predictor for poor neurological outcome, with a 43% sensitivity and no false positives⁴. In contrast, in several other studies TBI patients were described with initially bilateral absent N20 responses who regained consciousness and had only minor disabilities^{1,15,16}. These results show that absence of cortical SSEP responses is not a reliable predictor in TBI patients. The most likely explanation is that in head trauma, a transient N20 disappearance may be consecutive to focal midbrain dysfunction due to oedema¹. Therefore, SSEPs should never be used as a single test in TBI patients, but integrated with other neurophysiologic tools and clinical examination to improve the predictive value^{1,14,15}. In TBI patients it is especially important to rule out traumatic lesions of the peripheral nerves, nerve roots or spinal cord when using clinical neurophysiologic tests. Clinical examination of the peripheral nerves can be difficult in patients with a diminished consciousness.

Subarachnoid haemorrhage

In patients with subarachnoid haemorrhage, neither median or tibial nerve SSEP, flash-visual evoked potential, BAEP nor central conduction time of the median nerve SSEP can be used as a valid predictor for outcome. The patient's initial clinical grading still provides the only satisfying predictor, independent of the patient's clinical course¹⁷.

Sepsis

In patients with severe sepsis and septic shock, prolonged cortical SSEP peak latencies occur in 84% of the patients. These prolonged

latencies can be used to diagnose septic encephalopathy and its severity is associated with the severity of illness¹⁸. In these patients SSEP cannot be used to determine prognosis.

Pitfalls and limitations of SSEPs at the ICU

Noise

The most severe limitation of the SSEP is the moderate interobserver agreement, which is extensively described in a study of Zandbergen et al.¹⁹. In their study, SSEPs of 56 consecutive patients with anoxic–ischaemic coma were interpreted independently by 5 experienced clinical neurophysiologists. The interobserver agreement for SSEPs in anoxic–ischaemic coma was only moderate (kappa 0.52, 95% CI 0.20–0.65). The main source of disagreement was related to the noise levels. For recordings with a noise level of 0.25 μ V or more, mean kappa was 0.34 (fair agreement); for recordings with a noise level below 0.25 μ V mean kappa was 0.74, which is a substantial agreement¹⁹.

Efforts should be made to improve the registration and diminish noise as much as possible. Zandbergen et al. recommend that the peak-to-peak amplitude of noise of the cortical and cervical leads should be lower than 0.25 μ V after averaging, especially in the frequency of the SSEPs themselves (20–500 Hz)¹⁹. Giving muscle relaxants can often improve the quality of the SSEP in patients with too much muscle activity; an example is given in *figure 2*. Furthermore, disturbing electrical ICU equipment should be turned off if possible. Also, giving more stimuli (up to 1000 or more) and increasing the stimulus intensity could improve the signal-to-noise ratio¹⁹. Since the interpreting clinician is often not present during the actual SSEP registration itself, the role of the lab technician is crucial in obtaining reliable SSEP results. As the quality of the SSEP recording depends on the skills of the technician, it is important that they are well trained and sufficiently familiar with SSEP registrations in the ICU. In those situations where significant artifacts appear to be present, the referring physician should be informed. Furthermore, it is always the role of the interpreting clinician to check the quality and signal-to-noise ratio of the SSEP registration, and to decide

whether the SSEP registration is reliable enough for clinical decision making.

Interpretation Criteria

Despite the noise level, also other criteria for reliable results can be given. An N20 peak on one side can only be considered as present if it fulfils all the following criteria:

- It should have an appropriate latency (i.e. at least 4.5 ms longer than the corresponding N13 peak in normal-stature adults)¹⁹.
- It should be present on the contralateral side, and there should be a clear difference with the recording from the side ipsilateral to the stimulus¹⁹. Therefore it is recommended to record not only the contralateral sensory cortex after stimulation, but also co-register the ipsilateral side. This prevents misinterpretation of the N18, which has its origin in the brainstem, as a N20 potential.
- Any potentials found should be reproducible in a second set of stimuli^{1,19}.

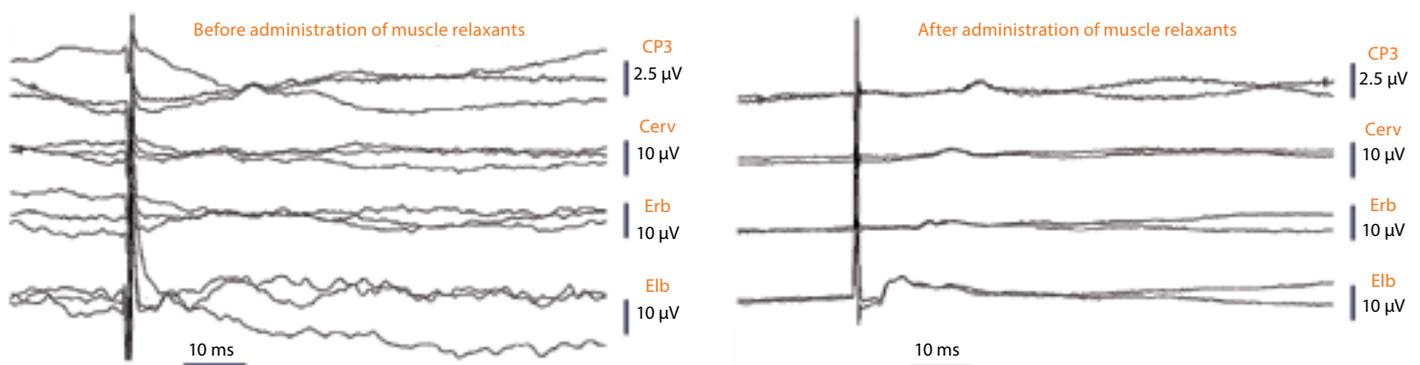
Bilateral absence of N20 peaks requires the presence of normal potentials over Erb's point and the neck (N13) to ensure that the impulses have arrived in the central nervous system^{1,19}.

Disturbing factors and sedation

Cortical responses are not influenced by moderate sedation or metabolic disturbances, factors that often hamper clinical neurological examination in the ICU. However, intoxication or metabolic disturbances and other explanations for absent SSEP potentials, for example a high cervical lesion, should be ruled out.

The N20 is relatively independent to the level of sedation, and remains present even at a sedation level that is sufficient to induce an isoelectric EEG^{1,19}. Propofol produces minimal to less than 10% suppression of the SSEP amplitude^{20–23}. Also midazolam and opioids have only moderate effect on the SSEP amplitude and latency^{20–23}. Furthermore, remifentanyl can suppress the cortical SSEP components by 20–80%, when given in a high dose (0.8 μ g/kg/min) as used during neuromonitoring in the operation room²⁰. On the other hand, in a small percentage of cases it may be even useful to

Figure 2. Example of the effect of Esmeron on a SSEP after stimulation of the right n. medianus in a patient after resuscitation. The evoked potential is measured cortical (CP3), cervical (Cerv), at Erb's point and at the elbow (Elb)



give sedation in low dose to improve the quality of the SSEP. This is especially the case in patients with generalized periodic discharges, which in some situations can be suppressed after administration of propofol. These periodic discharges often have large amplitudes in comparison to the evoked potential and can disturb the cortical response. An illustration of a positive effect of propofol on the quality of the SSEP recording is given in *figure 3*.

Discussion

Prognostication of comatose patients in the ICU using clinical examination is often difficult and neurophysiological assessment may assist in clinical decision making. The SSEP is a relatively simple, inexpensive, and non-invasive method to evaluate functional damage to the complete sensory pathway from the peripheral nervous system, dorsal column of the spinal cord, lemniscal pathways in the brainstem, with eventual arrival at the somatosensory cortex.

The SSEP can be used in the prediction of the neurological outcome in comatose patients with different aetiologies. However, it is only sufficiently reliable in predicting poor neurological outcome in patients with a post-anoxic coma, although the sensitivity for predicting a poor outcome is relatively low. For the prediction of a favourable neurological outcome the SSEP cannot be used. Other neurophysiologic tools, such as continuous EEG¹³ and the mismatch negativity and P300 responses^{24,25} may provide additional or even improved information in these cases.

In TBI patients, SSEPs can assist in the prognosis, but should never be considered in isolation but integrated with other neurophysiologic tools and clinical examination. In patients with subarachnoid haemorrhage or sepsis the SSEP has no prognostic value.

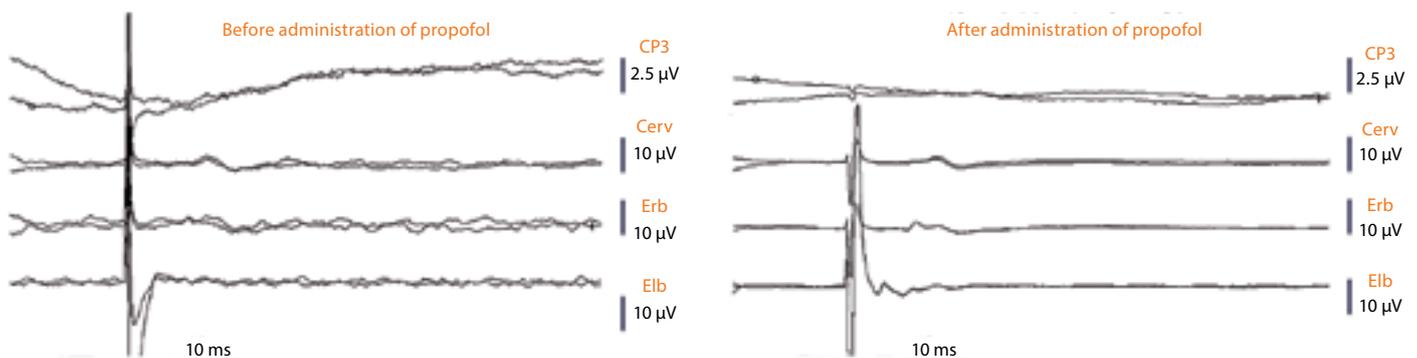
Since the SSEP is usually recorded for prognostication, absent cortical responses almost always lead to withdrawal of intensive care treatment, the clinician interpreting the results of the SSEP recording has to be 100% certain. Decisions to withdraw treatment are irreversible and therefore the N20 SSEPs should be considered as 'not bilaterally absent' in cases of doubt.

In conclusion, the SSEP is a very reliable and reproducible method, if it is performed and interpreted correctly. A bilateral absent N20 response is a reliable predictor for poor neurological outcome in patients with a postanoxic coma. In postanoxic patients treated with hypothermia, the SSEP can reliably be measured after rewarming and probably also during the period of hypothermia. In other comatose patients, such as TBI patients or patients with a subarachnoid haemorrhage, the SSEP measurement is not reliable enough for the prognosis of poor outcome to use as a single parameter in clinical decision making. During SSEP measurements great care should be taken in improving the signal to noise ratio. If the noise level is too high, the peripheral responses are abnormal, or the response is not reproducible in a second set of stimuli, interpretation of the SSEP cannot be done reliably and the SSEP should be measured again in a later stage.

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Figure 3. Example of the effect of Esmeron and Propofol on a SSEP after stimulation of the right n. medianus in a patient after resuscitation. The evoked potential is measured cortical (CP3), cervical (Cerv), at Erb's point and at the elbow (Elb). Before administration of propofol the EEG showed generalized periodic discharges, while after the administration of propofol the EEG showed diffuse delta activity



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