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Original Article

Uncertainty of somatosensory evoked potentials during neurosurgical procedure

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The objective of measurement of bio-signals in measurement uncertainty is not to determine the true value as closely as possible, but to determine a measured value and to assign the interval of the value. The measurement uncertainty is estimated by type A and B evaluations, depending on whether they are evaluated by statistics or the mathematical probability theory. Intraoperative neurophysiologic monitoring is used often for early detection of inherent risk relevant to neurosurgical procedures leading to permanent neurological injury, while it is still potentially reversible. In this study, we evaluated the uncertainties in somatosensory evoked potentials (SSEPs), which are used for monitoring sensory neural pathways. In a 45-year-old man who underwent cervical laminectomy, SSEPs were monitored using the ISIS IOM SYSTEM (Inomed, Emendingen, Germany) to evaluate the uncertainties. Expanded uncertainty were 0.88 mV and 1.22 ms, for amplitude and latency, respectively. Measured values and corresponding uncertainties of amplitude and latency were 2.78 ± 0.88 mV and 24.02 ± 1.22 ms, respectively. The expanded uncertainty (0.88 mV) of the amplitude was approximately 30% of the mean value (2.78 mV). A reasonable explanation for this would be the effects of variables such as electromagnetic waves (diathermy and warming blankets), temperature, blood pressure, sex and body mass index on SSEPs. Careful attention is required in interpreting SSEPs.

Key words: uncertainty, bio-signals, intraoperative neurophysiologic monitoring, somatosensory evoked potentials, sensory neural pathway

Introduction

Intraoperative monitoring of somatosensory evoked potentials (SSEPs) has gained popularity over the past decades as it enables monitoring the functional integrity of sensory neural pathways in anesthetized patients during aortic, spinal or brain stem surgeries. While these surgical procedures may place the sensory pathways at risk, the application of SSEPs for this purpose is based on its reliability for detecting ischemic spinal cord dysfunction or nerve injuries. Evoked potentials (EPs) are recorded by stimulating peripheral sensory organs or nerves, and recording the resulting central nervous system (CNS) manifestations expressed as electrical potentials. As EPs have a very low amplitude, and the simultaneous electroencephalogram (EEG) and electromyogram (EMG) waves are relatively high, signal averaging and summation techniques are used for EPs to be extracted from the background EEG, EMG waves, artifacts. There are different types of EPs as follows: visual evoked potentials (VEPs), brain stem auditory evoked potentials (BAEPs), SSEPs, and motor evoked potentials (MEPs). SSEPs are recorded by stimulating the peripheral sensory nerves (mainly the median nerve or the posterior tibial nerve) and extracting electrical potentials at various sites along the sensory pathways to the cerebral cortex or the scalp.

SSEPs can be clinically used in a variety of neurological disorders, particularly, in neurosurgical procedures such as spinal surgeries during anesthesia in an attempt to prevent neurological injuries. Although anesthetized patients are monitored using SSEPs during a many neurological surgeries such as on the brain (brain stem surgeries, resection of thalamic [1] and acoustic tumors [2], vascular lesions involving the sensory cortex [2]), the spine (surgical correc-

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tion of spinal deformities (scoliosis, or kyphosis)) [3, 4], spinal cord decompression [5, 6], resection of spinal cord tumors [2], and fusion [7]), and for thoracic and abdominal aortic aneurysm repair [8], the interpretation of SSEPs mainly depends on the observer's subjective real-time assessment of the sensory neural pathways function. More over, statistical techniques (such as standard deviation (SD), standard error of the mean (SEM)) that are widely used cannot guarantee the reliability of SSEPs measurement. Measurement uncertainty characterizes the dispersion of the quantity values being attributed to a measurand based on the information used. It is evaluated by type A and B uncertainties that can be characterized and evaluated by statistical distribution and probability density [9].

In this study we studied the sources of uncertainties of amplitudes and latencies of SSEPs and evaluated their uncertainties for an anesthetized patient undergoing spinal surgery according to Guide to the expression of Uncertainty in Measurement (GUM) [9].

Materials and Methods

Following the institutional review board (IRB) approval (IRB FILE NO 2018-10-001-001), SSEPs were monitored using the ISIS IOM SYSTEM (Inomed, Emendingen, Germany) to calculate uncertainties (RESULTS for details) in a 45-year-old man undergoing cervical laminectomy.

Measurement of sensory neural action potentials and measurands

Sensory neural action potentials (SNAPs) were measured and measurands (amplitudes and latencies) were calculated using the measurements of SNAPs in each montage (Channel 1: CPc-CPi, Channel 2: CPi-Ref, Channel 3: C5S-Ref, Channel 4: Epi-Ref).

Measurement procedures

Total intravenous anesthesia (TIVA) was administered using propofol and remifentanil. The temperature was maintained within the normal range (normothermia, 36℃–37℃) during the entire study period. Complex nerves (median and posterior tibial nerves) of the upper and lower extremities were electrically stimulated with a constant voltage. Measurands of SNAPs (amplitudes and latencies) were measured in the bi-temporal areas of C3 and C4 on the scalp.

Calculation of uncertainties

The standard uncertainties of type A evaluation based on five measurements of SNAPs, type B evaluation on the resolution of the equipment and type B evaluation based on the calibration result. The combined standard uncertainty (u_c) and expanded uncertainty (U) were calculated following the described protocols.

Uncertainties of amplitude (mV)

Mathematical models of amplitude measurement

A, the amplitude of SSEPs, measured using the ISIS IOM SYSTEM, can be described as follows.

$$A = A\mathrm{p} + C_A$$

Ap is the amplitude of SSEPs in a patient, and C_A is the uncertainty of correction for a systematic effect obtained from calibration.

$$u_c(A) = \sqrt{u(A\mathrm{p}_{\ \mathrm{repeatability}})^2 + u(A\mathrm{p}_{\ \mathrm{resolution}})^2 + u(C_A)^2}$$

$u_c(A)$: combined standard uncertainty
$u(A\mathrm{p}_{\ \mathrm{repeatability}})$: uncertainty of measurements
$u(A\mathrm{p}_{\ \mathrm{resolution}})$: uncertainties due to the resolution of the equipment
$u(C_A)$: uncertainties based on the calibration of the equipment
U_A: *expanded uncertainty*

Uncertainties of latency (ms)

Mathematical models of latency measurement

L, the latency of SSEPs, measured using the ISIS IOM SYSTEM, can be described as follows.

$$L = L\mathrm{p} + C_L$$

Lp is the amplitude of SSEPs in a patient, and C is an uncertainty of correction of systematic effect.

$$\mathrm{u_c(L)} = \sqrt{u(L\mathrm{p.}_{\ \mathrm{repeatability}})^2 + u(L\mathrm{p.}_{\ \mathrm{resolution}})^2 + u(C_L)^2}$$

$u_c(L)$: combined standard uncertainty
$u(L\mathrm{p}_{\ \mathrm{repeatability}})$: uncertainty of five measurements
$u(L\mathrm{p}_{\ \mathrm{resolution}})$: uncertainties based on the resolution of the equipment
$u(C_L)$: uncertainties based on the calibration of the equipment
U_L: *expanded uncertainty*

Calibration uncertainty for amplitude and latency, of type B, was calculated based on the calibration data (measurement uncertainty) of the equipment provided by the manufacturer. If the results of the probability distribution of measurement show a normal distribution or a t-distribution with effective degrees of freedom over ten for expanded uncertainty, the combined standard uncertainty is multiplied by k (= 2) conventionally (level of confidence = 95%).

Results

Uncertainties (amplitude in mV and latency in ms, respectively), of type A ($u(Ap_{\text{repeatability}}) = SD/\sqrt{5}$ mV, $u(Lp._{\text{repeatability}}) = SD/\sqrt{5}$ ms) based on five measurements, type B ($u(Ap_{\text{resolution}}) = 0.005$ mV $/\sqrt{3}$, $u(Lp_{\text{resolution}}) = 0.005$ mV $/\sqrt{3}$) based on the resolution of the equipment, type B ($u(C_A)$ = measurement uncertainty/2, $u(C_L)$ = measurement uncertainty/2, (measurement uncertainty = 0.4 mV and 0.2 ms)) based on the calibration of the equipment (calibration uncertainty), combined standard uncertainty ($u_c(A) = \sqrt{u(Ap_{\text{repeatability}})^2 + u(Ap_{\text{resolution}})^2 + u(C_A)^2}$, $u_c(L) = \sqrt{u(Lp._{\text{repeatability}})^2 + u(Lp._{\text{resolution}})^2 + u(C_L)^2}$) and expanded uncertainty ($U_A = 2 \times u_c((A)$, $U_L = 2 \times u_c(L)$) were 0.34 mV (2.78 ± 0.76) and 0.61 ms (24.02 ± 1.36), 0.003 mV and 0.003 ms, 0.2 mV and 0.1 ms, 0.44 mV and 0.61 ms, and 0.88 mV and 1.22 ms, respectively (Table 1 and 2). Measurement results of amplitude and latency were 2.78 ± 0.88 mV and 24.02 ± 1.22 ms, respectively. The expanded uncertainty (0.88 mV) of the amplitude was nearly 30% of the measured value (2.78 mV).

Discussion

Intraoperative neurophysiologic monitoring is often used for the early detection of inherent risk relevant to neurosurgical procedures leading to permanent neurological injuries, while they are still potentially reversible. Intraoperative neurophysiologic monitoring uses the following four modalities of EPs: BAEPs, VEPs, SSEPs, and MEPs. While amplitude and latency are the only measurands of EPs measuring neural function and integrity, there are many confounding factors resulting in uncertainty of the changes in amplitude and latency. Because of these factors it is very challenging to develop standards of EPs stimulation and interpretation, for reliable prediction of the degrees of neurological deficits. This study aims to propose useful stimulus settings and optimization of monitoring condition to minimize the uncertainty of EPs.

Table 1. Uncertainty budget for amplitude

Sources of uncertainty	Standard uncertainty for amplitude (mV)	Type	Probability distribution
$u(Ap)$	0.34	A	Normal
$u(Ap._{\text{repeatability}})$	0.34		
$u(Ap._{\text{resolution}})$	0.003		
$u(Ap._{\text{resolution}})$	0.003	B	Rectangular
$u(C_A)$	0.2	B	Normal
$u_c(Ap)$	0.44		Assumed as rectangular
$U(Ap)$	0.88		Assumed as rectangular

Table 2. Uncertainty budget for latency

Sources of uncertainty	Standard uncertainty for latency (ms)	Type	Probability distribution
$u(Lp)$	0.61	A	Normal
$u(Lp._{\text{repeatability}})$	0.61		
$u(Lp._{\text{resolution}})$	0.003		
$u(Lp._{\text{resolution}})$	0.003	B	Rectangular
$u(C_L)$	0.1	B	Normal
$u_L(Ap)$	0.61		Assumed as rectangular
$U(Lp)$	1.22		Assumed as rectangular

The current study aimed to assess the uncertainty of the equipment (ISIS IOM system) used for monitoring SSEPs. We were able to retain the metrological traceability using the calibration data provided by the manufacturer. SSEPs are considered to detect significant abnormalities during sensory neural transmission processes. As a result, the integrity of the pathway at risk can be monitored and the surgeon can reduce insults to the compromised neuronal tissues and improve perfusion of these structures. For detection of abnormalities in SSEPs, the latency and amplitude are measured and an increase of 50% and/or a drop of more than 10% are considered significant changes. Therefore, how close the measurement results (measurands) are to the true value to be measured is very important. This concept of measurement has been described by the term uncertainty. The purpose of measurement in the uncertainty approach is not to determine a true value as closely as possible. Preferably, the information from a measurement permits the assignment of an interval of reasonable values of the measurand based on the assumption that no mistakes have been made during the the measurement [9]. In this study, it was noted that expanded uncertainty (0.88 mV) of the amplitude was approximately 30% of the measured value (2.78): measurement results of amplitude and latency were 2.78 ± 0.88 mV and 24.02 ± 1.22 ms, respectively. Type A (0.34 mV, five measurements) uncertainty in amplitude was considered to influence the total uncertainty (combined standard uncertainty and expanded uncertainty) greater than type B uncertainties. A reasonable explanation for this would be the influence of variables such as electromagnetic waves (diathermy and warming blankets), temperature, blood pressure, sex, BMI, etc on SSEPs. Careful interpretation is required for interpreting SSEPs.

A number of medical devices used in operating theaters

such as electric surgical units (diathermy), temperature-regulating water blankets and fluid warmers can affect the measurements of SSEPs by increasing artifacts or by adding noises. In addition, electric current and fluorescent glow from other theater equipment may also influence sensory modalities. Thus, to reduce the interference of equipment on the electric and magnetic fields the connection between electrodes and ground connections (earth) should be ensured. Furthermore, the SSEPs monitor needs to be more than two meters away from electromagnetic equipment.

There are a number of anesthetic drugs used during the perioperative period can influence the intraoperative monitoring of SSEPs with varying effects depending on the drug classes (volatile agents, intravenous agents, or opioids). SSEPs and MEPs that measure the reaction of a living body by offering an external electrical stimulus are highly affected by volatile anesthetic agents. Although these modality potentials are depressed at 1 MAC (minimum alveolar concentration) the currently used volatile agents dose-dependently decrease the amplitude and increase the latency of SSEPs [10-12]. For this reason anesthesia based on intravenously applied drugs is commonly recommended for intraoperative monitoring of SSEPs. Although the administration of propofol causes dose-dependent increases in amplitude, it does not have a large effect on latency. Opioids, in general, produce dose-dependent changes in SSEPs but clinical doses can be used in patients requiring SSEPs intraoperatively without impairing the ability to monitor the neurologic function adequately [13, 14]. A neuromuscular blockade has been demonstrated to have large effects on MEPs but not on SSEPs.

Temperature also affects SSEPs. Hypothermia causes the delay of the revelation of electrical potentials and tends to increase the stimulation threshold with loss of the waves at temperature below 28℃ [15]. Hyperthermia also alters SSEPs in a similar manner at 42℃ [16]. These studies showed that temperature should be maintained within the normal range of the body temperature ±2.5℃ for intraoperative monitoring of SSEPs.

Regional administration of local anesthetics (subarachnoid block) abolishes SSEPs by complete block of the sensory neural pathway [17]. Local infiltration of local anesthetics may also have the similar effects on SSEPs [18, 19]. However, epidural block using local anesthetics variably influences SSEPs [20, 21].

There are also a number of variables that may exert a large or small influence on SSEPs. They include anthropologic factors (age, gender, and race), physiologic factors (blood pressure and blood flow), physical factors (body mass index, length of the limbs), surgical diseases and a state of disease such as increased intracranial pressure, and external factors (electric current, examination time, and personal interpretation technique).

In conclusion, measurement results of amplitude and latency were 2.78 ± 0.88 mV and 24.02 ± 1.22 ms, respectively. The expanded uncertainty (0.88 mV) of the amplitude was about 30% of the measured value (2.78 mV). This may be the influence of variables such as electromagnetic waves (diathermy and warming blankets, etc), temperature, blood pressure, gender, and BMI on SSEPs. Thus, meticulous attention is required in interpretation of SSEPs. This also suggests that uncertainty in SSEPs measurement needs to be minimized by reducing the effects of the above mentioned variables in evaluating the possibility of neurological injuries.

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