Original Article

Reliability of perioperative SSEP recordings in spine surgery

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Objective: The reproducibility and clinical reliability of perioperative somatosensory-evoked potentials (SSEP) were prospectively evaluated in uneventful scoliosis surgery. The influence of anesthesia owing to induction of total intravenous anesthesia (TIVA) upon preoperative SSEP and the variability of intraoperative SSEP were calculated. The potential effect of spine surgery was assessed by comparing pre- to postoperative SSEP.

Methods: A total of 2143 pre-, intra- and postoperative tibial and median SSEP recorded in 25 patients undergoing spine surgery owing to idiopathic scoliosis were analyzed. The anesthesia protocol consisted of a computerized target controlled infusion (TCI) device for propofol and intravenous application of an opioid.

Results: Anesthesia induced a significant and comparable prolongation of the tibial SSEP onset, P40 and P60 latencies, while the N50 latency was less changed. Throughout anesthesia, latencies of median (onset, N20, P25 and N35) and tibial (onset, P40, N50 and P60) SSEP showed mean variations of less than 6%. The intraoperative SSEP amplitudes were less stable with a relative standard deviation of 30–40%. In uneventful spine surgery, the postoperative tibial SSEP were not significantly changed in comparison to preoperative recordings.

Conclusions: By using a standardized anesthesia protocol, the impact of anesthesia on preoperative SSEP can be predicted. Furthermore, the controlled application of sedatives and analgesics allows recording of stable SSEP parameters for intraoperative monitoring purposes. As in uneventful spine surgery pre- to postoperative SSEP are unchanged the latter comparison can be applied as an additional perioperative neuromonitoring procedure to assess the influence of spine surgery or other invasive interventions on spinal cord function.

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Introduction

During spine surgery, that is, scoliosis, neurological deterioration may result from compression, stretching, vascular insufficiency or direct trauma of the spinal cord by instrumentation.^{1–3} To most of these complications, the surgeon is lacking intraoperative reliable warning criteria. To manage this limitation, the Stagnara wake up test is recommended, which, however, reveals inherent serious disadvantages like delayed diagnostic information, time-consuming procedure and discomfort for the patient.^{4–6} To overcome these problems, somatosensory evoked potentials (SSEP) have been introduced for neurological investigation and monitoring of the

integrity of the neural pathways during surgical procedures. This technique allows an on-line surveillance and early diagnosis of spinal cord dysfunction and aims to provide warning signals before an irreversible damage has occurred. Owing to the sensitivity and specificity of SSEP monitoring, the incidence of postoperative paraplegia can be significantly reduced.^{3,7–10}

However, a reliable intraoperative monitoring demands appropriate procedures of anesthesia, since the anesthetic itself, as well as accompanying hypothermia and hypotension, have a serious influence on evoked potentials. The depressant effect of volatile anesthetics on evoked potentials is well known.^{11–13} While low-dose volatile anesthetics in combination with an opioid is considered as appropriate anesthesia for monitoring purpose, recent studies evaluated the performance of

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total intravenous anesthesia (TIVA) for intraoperative neuromonitoring with the combination of propofol and fentanyl.^{3,12–18}

TIVA in combination with a target-controlled infusion (TCI) device allows the determination of the amount of applied propofol and the estimation of the plasma propofol concentration. This allows long-lasting anesthesia and the possibility of comparable anesthesia.^{17,19,20}

In the present study, the clinical reproducibility and reliability of pre-, intra- and postoperative SSEP recordings were assessed in uneventful scoliosis surgery. Firstly, the impact of anesthesia was calculated in an intersubject comparison of SSEP parameter differences between preoperative and intraoperative SSEP. Secondly, the intraoperative within-case variabilities of SSEP parameters were calculated, statistically analyzed and compared to available data in literature. Thirdly, to estimate the impact of surgical procedures and anesthesia on SSEP, postoperative SSEP were compared to the preoperative SSEP. The analysis of data should outline which SSEP markers can be applied for reliable perioperative (pre–intra–postoperative) monitoring as especially the suitability of postoperative SSEPs in the assessment of spinal cord function after spine surgery is not yet established.

Methods

Patients

In a prospective study, pre-, intra- and postoperative SSEP of 25 patients (mean age 16 (± 8) years, range of 6–48 years; females to males = 23:2) suffering from idiopathic scoliosis (26 surgical interventions performed between 1997 and 1999) were analyzed. Approval of the local ethic commission was achieved. Only patients suffering from idiopathic scoliosis (mean Cobb angle 60 (± 11)°) without evidence of a neurological impairment, based on a full neurological examination, were included. In all patients, additional intraspinal lesions besides spinal deformity were excluded by radiological workup (X-ray and MRI).

In all patients a postoperative full neurological re-examination was performed to ascertain an unchanged normal neurological condition after spine surgery.

SSEP protocol

In all patients, multiple perioperative SSEP recordings consisting of pre-, intra- and postoperative measurements were performed. Preoperative tibial SSEP of the right and left lower limb were recorded 1 day before operation, while the postoperative control of tibial SSEP (at the same conditions as the preoperative SSEP) was performed in about 7 days (range 4–12 days) after spine surgery. Intraoperative monitoring consisted of median and tibial SSEP (left and right side) in parallel, in which the median SSEP was acting as a control for the tibial one.

For intraoperative assessment, a total of 2049 intraoperative SSEP measurements of 25 patients

Figure 1 Comparison of pre- and intraoperative tibial SSEP showing the mean changes during stable anesthesia. According to the international nomenclature, positive peaks are represented by downward deflections and labeled P and negative peaks are represented by upward deflections and labeled N. The following latencies were measured: P40 (=P1), N50 (=N1), P60 (=P2) and N75 (=N2). Amplitudes were measured baseline to peak for onset-P1 and peak to peak for the other amplitudes (P1–N1 and N1–P2)

undergoing 26 surgical interventions were analyzed; a mean average of 13 (± 6) SSEP recordings of each median nerve and 26 (± 14) of each tibial nerve were performed per operation.

For comparison of pre- to intraoperative SSEP, the preoperative left and right tibial SSEP of the same 25 patients were individually compared to the corresponding averaged intraoperative tibial left and right SSEP.

Of the 25 patients, 21 underwent a postoperative control SSEP to compare the pre- to postoperative SSEP (42 tibial (21 left/21 right) postoperative SSEP were compared to the corresponding 42 preoperative tibial SSEP).

For calculation procedures, SSEP parameters were labeled the following way: P1, N1, P2 and N2 corresponding to P40, N50, P60 and N75, respectively, for tibial SSEP and N1, P1, N2 corresponding to N20, P25 and N35, respectively, for median SSEP.

For calculation of SSEP latency changes, latencies (onset, P1, N1, P2 and N2) as well as interpeak latencies (onset–P1, P1–N1, N1–P2 and P2–N2) were determined. The size of amplitudes was calculated by baseline to first peak and peak to peak for the remaining markers. Figure 1 shows the position of the tibial SSEP markers. All markers were set by a single person to reduce variability. He was blinded for the patients history, operative procedures and statistical analysis.

SSEP recordings

The tibial and median SSEP were elicited by electrical stimulation (square-wave stimulation of 200 μ s at a frequency of 3 Hz) at the ankle or wrist (using surface electrodes in pre-/postoperative stimulation and needle electrodes during operation; proximally placed cathodes, the anode places 2 cm distally) by a conventional

Table 1 Comparison of pre- and intraoperative tibial SSEP

	<i>Preop.</i>		<i>Intraop.</i>		<i>Percentage diff.</i> (intra-pre)		<i>Delta</i> (intra-pre)			
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean (%)</i>	<i>SD (%)</i>	<i>Mean</i>	<i>SD</i>	<i>Significant difference?</i>	<i>Correlation pre- to intraop.</i>
<i>Latency</i>										
LatOn	31.88	± 2.78 ms	34.35	± 3.42 ms	7.04	± 5.11	2.24	± 1.70 ms	Yes	Yes
LatP1	36.72	± 2.70 ms	37.84	± 3.67 ms	2.81	± 6.37	1.02	± 2.25 ms	Yes	Yes
LatN1	46.05	± 3.44 ms	46.43	± 5.31 ms	0.55	± 8.44	0.30	± 3.99 ms	No	Yes
LatP2	57.11	± 6.42 ms	65.50	± 7.31 ms	15.69	± 13.45	8.52	± 7.92 ms	Yes	Yes
<i>Inter peak latency</i>										
LatOn-P1	4.84	± 1.45 ms	3.42	± 1.14 ms	-20.63	± 31.89	-1.22	± 1.63 ms	Yes	Yes
LatP1-N1	9.33	± 2.88 ms	8.59	± 3.31 ms	-6.16	± 31.44	-0.72	± 3.07 ms	No	Yes
LatN1-P2	11.06	± 4.27 ms	18.99	± 4.48 ms	104.68	± 128.02	8.22	± 6.38 ms	Yes	No
<i>Amplitude</i>										
AmpOn-P1	3.52	± 3.13 uV	0.94	± 0.60 uV	Not calculated due to different recording technique					
AmpP1-N1	5.83	± 5.10 uV	1.79	± 1.10 uV						
AmpN1-P2	4.01	± 2.35 uV	1.34	± 0.79 uV						

Mean and standard deviation of pre- and intraoperative tibial SSEP latencies and amplitudes are listed. The influence of anesthesia on SSEP was assessed by calculating the absolute (ms) and relative (%) difference of latencies (level of significance: $P < 0.05$ for correlation and $P < 0.016$ for pre- to intraoperative comparison)

EMG machine (Dantec Keypoint[®], Medtronic Functional Diagnostics, Denmark for pre-/postoperative recordings; Neurowacs[®], Inomed, Germany for intraoperative recordings). Stimulation intensity in the awake patient was chosen two to three times above the sensory threshold, while during surgery at least 30 mA was applied to induce reproducible SSEP responses.

For recording, scalp electrodes (cup electrodes for pre-/postoperative recordings and needle electrodes for intraoperative recordings) were applied at Cz'/Fz and C3'/C4'/Fz using the International 10/20 electrode system. The electrode impedance was maintained below 5 kΩ. The amplifier was set at 5 μV/division, frequency bandpass was set at 50–2000 Hz. Two sets of 500 replications were averaged to improve the signal-to-noise ratio for latency and amplitude measurements.

Anesthesia

All surgical procedures were performed using TIVA. The patients were premedicated with oral 0.1 mg/kg body weight midazolam (Dormicum[®], Roche, Basel, Switzerland). After preoxygenation, anesthesia was induced with intravenous propofol (Disoprivan[®], Astra Zeneca, Zug, Switzerland) 4–6 mcg/ml blood concentration using a TCI device based on the pharmacokinetic data set from March and Gepts until loss of consciousness.²¹ Muscle relaxation was obtained for tracheal intubation by a single intravenous dose of 0.8 mg/kg body weight rocuronium (Esmeron[®], Organon Technika AG, Pfäffikon, Switzerland). No other muscle relaxation was performed during the whole surgical procedure. Analgesia was provided 2 min before intubation with intravenous 0.2 mg fentanyl (Sintanyl[®], Sintetica, Mendrisio, Switzerland), with repeated increments of 0.1 mg during surgery in order to maintain

blood pressure and pulse measurements in a range of 80–120% of the baseline values. The maintenance of the anesthesia occurred at a fixed TCI value of 250% the noted effect site concentration at the time of loss of consciousness, providing a concentration over the known ED₉₉ for propofol anesthesia. After positioning for surgery (prone position or lateral position for dorsal or ventral surgical spine access, respectively), the FiO₂ was reduced from 1.0 to 0.4, unless higher values were needed in order to maintain a SpO₂ value over 95%.

For maintenance of stable body core temperature, perfusion warming and heating blankets were applied.

Statistics

Statistical evaluations were performed by using a SAS software package (SAS Institute Inc., Cary, NC, USA). To make the comparisons between the pre- and intraoperative and the pre- and postoperative SSEP, a paired *t*-test was used ($P < 0.016$ was considered as significant). Regression analysis was performed between pre- and intraoperative SSEP. A *t*-test was used to assess significant intraoperative variation of the SSEP. To evaluate the stability of intraoperative latencies and amplitudes, mean and relative standard deviations were calculated. To compare the intraoperative variation of the median and tibial SSEP, a Wilcoxon test was performed. If not otherwise noted, $P < 0.05$ was considered as significant.

Results

Influence of stable TIVA on preoperative tibial SSEP

After achieving a stable level of anesthesia, the comparison of pre- to intraoperative tibial SSEP was statistically analyzed for latencies and inter-peak

Figure 2 Corresponding values of pre- and intraoperative onset and N1 latencies are plotted, which reveal a comparable influence of anesthesia on intersubject tibial SSEP latencies

latencies. Owing to different recording technique (cup electrodes for preoperative versus needle electrodes for intraoperative recordings), amplitudes could not be statistically calculated.

Intraoperative tibial SSEP latencies (mean $\pm$ SD) of onset (31.9 ± 2.8 – 34.4 ± 3.4 ms), P1 (36.7 ± 2.7 – 37.8 ± 3.7 ms) and P2 (57.1 ± 6.4 – 65.5 ± 7.3 ms) were significantly prolonged, while the latency of N1 (46.1 ± 3.4 – 46.4 ± 5.3 ms) showed no significant changes (Figure 1, Table 1). Interpeak latencies showed no changes for P1–N1 (9.3 ± 2.9 – 8.6 ± 3.3 ms), while the

interpeak latency of onset –P1 (4.8 ± 1.6 – 3.4 ± 1.1 ms) and N1–P2 (11.1 ± 4.3 – 19 ± 4.5 ms) were significantly altered.

Intraoperative amplitudes were strongly reduced in comparison to preoperative recordings. Although the reduction of amplitudes should be induced by anesthesia, statistical analysis was not performed due to the different recording techniques. Analysis of variance and regression analysis for all the peak and interpeak latencies was performed to assess how far the changes of tibial SSEP parameters can be predicted. We found a significant and linear relation between pre- and intraoperative values for latencies and interpeak latencies of onset, P1 and N1, which allows a prediction of changes due to a stable level of anesthesia (Table 1 and Figure 2).

Intraoperative variability of SSEP

Absolute and relative mean standard deviations of median and tibial SSEP during spine surgery were analyzed to assess the variability of peak and interpeak latencies and amplitudes (Table 3).

In both tibial and median SSEP recordings, the variability of latency markers were in mean less than 4% and for interpeak latencies below 25%, which corresponds to less than 3 ms as absolute values. The amplitudes in general showed a higher variability. Mean changes of early SSEP amplitudes of onset –peak 1 and peak 1 –peak 2 were of about 30% for tibial and median SSEP. The late amplitude of peak 2 –peak 3 of tibial nerve revealed a variability in mean of about 150% in contrast to median SSEP of about 36% (Table 3).

To assess a difference in variability between median and tibial SSEP, the variability (SD) of the correspond-

Table 2 Comparison of pre- and postoperative SSEP by calculation of absolute (ms, μ V) and relative (%) postoperative changes (level of significance: $P < 0.016$).

	<i>Preop.</i>		<i>Postop.</i>		<i>Percentage diff.</i> (post-pre)		<i>Delta</i> (post-pre)		<i>Significant difference?</i>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean (%)</i>	<i>SD (%)</i>	<i>Mean</i>	<i>SD</i>	
<i>Latency</i>									
LatOn	31.88	±2.77 ms	32.83	±2.62 ms	2.30	±3.73	0.73	±1.19 ms	Yes
LatP1	36.72	±2.67 ms	37.22	±2.46 ms	0.68	±2.19	0.25	±0.82 ms	No
LatN1	46.05	±3.40 ms	46.42	±2.97 ms	1.22	±3.43	0.54	±1.54 ms	No
LatP2	57.11	±6.36 ms	57.42	±4.63 ms	1.94	±6.86	0.92	±4.09 ms	No
LatN2	71.38	±7.72 ms	71.20	±6.93 ms	0.89	±9.04	0.22	±7.15 ms	No
<i>Interpeak lat.</i>									
LatOn-P1	4.84	±1.45 ms	4.29	±1.78 ms	−11.72	±26.53	−0.66	±1.62 ms	Yes
LatP1-N1	9.33	±2.88 ms	9.00	±2.25 ms	1.92	±23.22	−0.33	±4.26 ms	No
LatN1-P2	11.06	±4.27 ms	10.76	±3.99 ms	8.24	±52.68	−0.26	±6.02 ms	No
LatP2-N2	15.00	±5.40 ms	13.68	±5.57 ms	2.60	±37.62	−0.68	±5.41 ms	No
<i>Amplitude</i>									
AmpOn-P1	3.52	±3.13 uV	2.90	±2.48 uV	−8.52	±36.37	−0.57	±1.30 uV	Yes
AmpP1-N1	5.83	±5.10 uV	5.20	±3.88 uV	9.10	±69.77	−0.53	±2.29 uV	No
AmpN1-P2	4.01	±2.35 uV	3.54	±1.90 uV	−6.15	±31.99	−0.58	±1.36 uV	Yes

Table 3 Analysis of the intraoperative median and tibial SSEP

	<i>Tibial</i>		<i>Median</i>		<i>Tibial</i>		<i>Median</i>		<i>Higher reproducibility</i>
	<i>Mean SD in %</i>	<i>SD (%)</i>	<i>Mean SD in %</i>	<i>SD (%)</i>	<i>Mean SD</i>	<i>SD</i>	<i>Mean SD</i>	<i>SD</i>	
<i>Intraoperative</i>									
<i>Latency</i>									
LatOn	2.57	±1.40	3.32	±1.67	0.87	±0.48 ms	0.55	±0.27 ms	Upper
LatPeak1	2.35	±1.23	2.75	±1.04	0.88	±0.46 ms	0.53	±0.19 ms	Upper
LatPeak2	3.90	±1.92	2.91	±1.62	1.80	±0.86 ms	0.70	±0.45 ms	Upper
LatPeak3	3.88	±3.15	5.41	±4.48	2.46	±1.79 ms	1.89	±1.87 ms	Upper
<i>Inter peak latency</i>									
LatOn-Peak1	21.60	±10.58	22.45	±11.84	0.73	±0.47 ms	0.54	±0.26 ms	Upper
LatPeak1-Peak2	19.26	±10.78	13.46	±7.27	1.60	±0.96 ms	0.55	±0.45 ms	Upper
LatPeak2-Peak3	13.88	±10.28	17.17	±13.87	2.37	±1.51 ms	1.72	±1.84 ms	Upper
<i>Amplitude</i>									
AmpOn-Peak1	31.14	±15.05	38.36	±15.83	0.25	±0.14 uV	0.25	±0.17 uV	No sign
AmpPeak1-Peak2	27.27	±14.38	27.73	±14.73	0.43	±0.22 uV	0.71	±0.37 uV	Lower
AmpPeak2-Peak3	155.09	±821.60	36.09	±19.07	0.51	±0.25 uV	0.91	±0.57 uV	Lower

ing peaks, interpeaks and latencies were compared by Wilcoxon test between the median and tibial SSEP.

All the peak and interpeak latencies (onset, peak 1, peak 2 and peak 3) were significantly ($P < 0.05$) more stable in the median SSEP (see Table 3).

While the variability of amplitude of onset –peak 1 did not show a difference between median and tibial SSEP, the amplitudes of peak 1 –peak 2 and peak 2 –peak 3 were significantly more stable in the tibial SSEP (Table 3).

Comparison of pre- and postoperative tibial SSEP

To assess the reproducibility of tibial SSEP after uneventful surgical treatment, corresponding SSEP obtained pre- and postoperatively were compared. Absolute changes of the calculated peaks (ms), interpeaks (ms) and amplitudes (μ V) and relative changes (%) were compared (Table 2).

The postoperative tibial SSEP showed only a significantly increased latency of onset of 0.73 ± 1.19 ms, while the other latency markers were not significantly changed. Comparison of the relative differences between pre- and postoperative SSEP showed that the mean changes of all the latencies, whether the difference was significant (onset) or not (P1, N1, P2 and N2), were less than 3%.

The amplitudes of onset –P1 and N1 –P2 were significantly reduced, while the amplitude P1–N1 was unchanged postoperatively. However, the mean changes of all the amplitudes were less than 10% compared to the preoperative values (Table 2).

Discussion

The assessment of sequential perioperative SSEP recordings (pre-, intra-, postoperative) in scoliosis surgery revealed several clinically relevant findings. Anesthesia by computer-assisted TIVA induces predictable changes

of tibial SSEP markers with valuable intraoperative variability of SSEP recordings. The reassessment of early SSEP markers (latencies and amplitudes of tibial SSEP) can be applied for postoperative follow-up examinations, as they remain unchanged in uneventful spine surgery. Therefore, perioperative SSEPs can be applied supplementary to clinical examinations, as postoperative follow-up recordings are able to assess the deterioration of spinal cord function due to surgical or systemic affections.

Although not extensively evaluated, it is assumed that preoperative SSEP are of limited use for monitoring purpose, as several factors are known to affect intraoperative SSEP (ie anesthetic drugs, reduced core temperature, hypotension).^{22–24} However, the present findings reveal that by application of computer-assisted TIVA characteristic changes of early SSEP components can be predicted. This allows to distinguish changes of intraoperative SSEP parameters, which are not induced by the anesthesia. The comparable intersubject levels of anesthesia due to the computer-assisted propofol application induces intraoperative SSEP changes that can be reliably predicted.^{18–20,25} The influence of midazolam used for premedication can be neglected, as several studies showed no or only a transient effect on SSEP latencies.^{22,26,27} Also the application of low doses of opioids (fentanyl) is not supposed to induce the predictable changes on SSEP latencies.^{18,22,28}

The intraoperative within-case variability of SSEP is of relevance in performing neuromonitoring during surgery.^{29–31} It is of importance to determine the range of SSEP variability, which can be expected due to specific protocols of anesthesia.³¹ This defines the borders for changes of latency and amplitude for giving relevant warning signals with high sensitivity and specificity to avoid false-negative and -positive warnings.²³ Comparing the within-case variability of intraoperative SSEP during scoliosis surgery, the performance of TIVA with application of propofol by TCI showed a

favorable low variability of early components competitive to volatile narcosis based on nitrous oxide plus opioid.²⁹ The within-case variability in serial intraoperative SSEP over 60 min in minor spine surgery under propofol in TIVA without computer-assistance showed a comparable extent.³¹ However, the presented results can only be indirectly compared to data published, as the within-case variability is also dependent on different disorders and clinical conditions.^{29,31–33} The evaluation of intraoperative SSEP variability by using interindividual comparison of SSEP was not applied in this study, as the intraindividual variability should be superior for monitoring purposes.^{33–35}

Comparing the intraoperative intraindividual variability of the median and tibial SSEP, a significant smaller variability of median SSEP latencies was found. Whether this difference is due to the different and longer pathways of the tibial SSEP or the influence of surgical procedure on spinal cord is questionable and there are no conclusive data in literature to this point.

The literature is sparse with regards to the influence of spine correction surgery of idiopathic scoliosis on preoperative tibial SSEP markers and the subsequent possibility of follow-up examinations.^{30,36} This study showed that early SSEP components are not significantly influenced by uneventful spine surgery and can therefore be used for follow-up examinations. This generally enables to assess if spinal cord function is affected by surgery or other invasive interventions. Furthermore, the preservation of spinal cord function can be documented by tibial SSEP in serial follow-up examinations which can be advantageous in specific patients after spinal deformity correction. Patients suffering from idiopathic scoliosis undergoing spine surgery are frequently adolescents and in time may develop neurological deficits due to other clinical diseases, where SSEP recordings can still be used for diagnostic purposes.

In conclusion, SSEP changes because of the effects of anesthesia are predictable and stable during surgery which allows to distinguish SSEP changes due to anesthesia from other compromises. As pre- to postoperative tibial SSEP are not changed in uneventful spine surgery, perioperative SSEP can be applied as an additional perioperative neuromonitoring procedure. This enables to distinguish changes of spinal cord function due to operative procedures from preoperative conditions, and also in time from potentially developing disorders not related to spine surgery.

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