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Differential Effects of Isoflurane on Human Median Nerve Somatosensory Evoked Potentials

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The effect of isoflurane on median nerve somatosensory evoked potentials (MN-SSEPs) was studied in 15 patients. Anesthesia was induced with thiamylal and maintained with oxygen and isoflurane. MN-SSEPs were recorded in awake patients and after achieving 0.5, 1.0, 1.5, and 2.0% stable end-tidal concentrations of isoflurane. Peak latencies and amplitudes of EP, N$\overline{13}$, and N$\overline{20}$ and conduction times EP-N$\overline{13}$, N$\overline{13}$-N$\overline{20}$, and EP-N$\overline{20}$ were measured. Peak latencies of all components increased after all concentrations of isoflurane compared with control values. N$\overline{20}$ peak latencies after 1% and 1.5% isoflurane differed significantly, whereas EP and N$\overline{13}$ latencies showed no significant difference. No significant change in conduction time EP-N$\overline{13}$ resulted from 1% and 1.5% concentrations of isoflurane compared with control values. Isoflurane increased conduction time N$\overline{13}$-N$\overline{20}$ significantly when compared with control values, and this increase was dose related. Amplitude of EP and N$\overline{13}$ did not show significant change with 1% and 1.5% isoflurane when compared with control values. Amplitude of N$\overline{20}$ decreased significantly following isoflurance anesthesia compared with control values, and the difference between 1% and 1.5% isoflurane recordings was also statistically significant. N$\overline{20}$ was not discernible in one out of 14 patients after 1.5% and in three out of ten patients after 2% isoflurane. These results indicate that subcortical potentials are less affected by isoflurane anesthesia than cortical potentials. Amplitude reduction of cortical potentials was more noticeable than either prolongation of peak latency or conduction time. The data suggest that in surgical procedures involving cervical spinal cord, intraoperative monitoring of MN-SSEPs is possible even with high concentrations of isoflurane, as N$\overline{13}$ can be reliably monitored. In procedures placing brain stem or cerebral somatosensory pathways at risk, where N$\overline{20}$ needs to be monitored, high concentrations of isoflurane should be avoided. (Key words: Anesthetics, volatile: isoflurane. Median nerve: evoked potentials. Monitoring: somatosensory evoked potentials.)

DESPITE A DRAMATIC INCREASE in the use of sensory evoked potentials (EPs) to monitor the integrity of neural pathways in anesthetized patients,[1] published information dealing with the effect of different anesthetic agents on short-latency somatosensory evoked potentials (SSEPs) is relatively limited. Early studies[2,3] indicated that most general anesthetics alter EPs, but these studies failed to provide information on quantitative effects of individual anesthetics on SSEPs. Many recent publications[4–6] have suggested that halogenated anesthetics should be avoided in patients in whom SSEPs are being monitored during surgery. No comparative study between all inhalation anesthetic agents and intravenous agents has been published so far. McPherson and co-workers[7] studied the effects of enflurane, isoflurane, and nitrous oxide on SSEPs during fentanyl anesthesia. They reported a greater decrease of amplitude of both upper and lower extremity evoked potentials after use of nitrous oxide compared to that with either enflurane or isoflurane. While their study challenges the commonly held belief that halogenated agents distort the EPs more than "balanced" anesthesia, they studied relatively low concentrations (0.25–1%) of isoflurane and enflurane, and their study did not describe the effect of these anesthetics *per se* on SSEPs. Further studies are needed to evaluate the effects of inhalation anesthetics on SSEPs.

We designed this clinical study to evaluate the use of isoflurane anesthesia in patients requiring monitoring of median nerve somatosensory evoked potentials (MN-SSEPs). We studied the differential effects of this anesthetic on the peripheral and central nervous system. We also evaluated a modification of MN-SSEPs monitoring technique so that halogenated anesthetics are not denied to patients who might otherwise benefit from their use.

Methods

The protocol was approved by the Committee to review investigations involving human beings at the University of Michigan, Ann Arbor. Fifteen consenting adult patients (six men and nine women) scheduled for elective surgery under general anesthesia were studied. Surgical procedures included exploratory laparotomy (4), mastectomy (1), vulvectomy (1), and lumbar laminectomy (9). The patients' mean age was 35 yr (range 20–52) with a mean weight of 60 kg (range 50.9–92.0) and mean height of 170 cm (range 156.5–187.5). All patients were evaluated preoperatively by an anesthesiologist and a neurologist and found free of systemic disease (ASA P.S. I) and neurologic disorders other than lumbar radiculopathy in patients undergoing laminectomy.

Control MN-SSEPs were recorded on the morning of

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TABLE 1. Order of Exposure to Different Concentrations of Isoflurane

End-tidal Concentration of Isoflurane (vol %)	Order in which a Particular Concentration was Administered				Total No. of Cases Studied with Each Concentration
	I	II	III	IV	
0.5	2	0	2	3	7
1.0	5	4	4	2	15
1.5	3	8	3	0	14
2.0	2	3	4	1	10

surgery in unpremedicated patients. Anesthesia was induced with intravenous thiamylal sodium (5–7 mg/kg), followed by either succinylcholine (1 mg/kg) or pancuronium bromide (0.1 mg/kg) to facilitate endotracheal intubation. Heart rate, ECG, systemic blood pressure, esophageal temperature, and end-tidal concentrations of carbon dioxide and isoflurane were continuously monitored during surgery. All patients were mechanically ventilated to maintain an end-tidal carbon dioxide tension of 35–40 mmHg. Anesthesia was maintained with 100% oxygen and isoflurane. MN-SSEPs were recorded at 0.5, 1.0, 1.5, and 2% end-tidal isoflurane concentrations. Intraoperative recording of MN-SSEPs began at least 20 min after injection of thiamylal sodium. End-tidal isoflurane concentration was held constant for at least 10 min before recording MN-SSEPs. The dose of isoflurane was administered according to needs of the patient (determined by changes in systemic blood pressure and heart rate) in keeping with the level of surgical stimulation. Therefore, not all patients could be studied at all concentrations, and the order of exposure to different concentrations of isoflurane varied, as shown in table 1. Recordings with 0.5% isoflurane were made either prior to surgical incision or at the end of surgical procedure. We could record MN-SSEPs at stable end-tidal isoflurane concentrations of 0.5% in seven, 1.0% in all 15, 1.5% in 14, and 2% in ten patients. We obtained recordings in only three patients at all four end-tidal concentrations of isoflurane, whereas 13 of 15 patients were successfully studied at both 1% and 1.5% concentrations. All patients were interviewed 24 h after surgery. None had recall of intraoperative events, and all patients expressed willingness to participate in a similar study again if necessary.

TABLE 2. Recording Technique Used for MN-SSEPs

Stimulation Parameters

- Site of stimulation: right or left median nerve at wrist
- Type of stimulation: percutaneous with disc electrodes
- Rate: 5.1/s
- Intensity: exceeding motor threshold
- Duration: 100 μs

Recording Parameters

Gain 10^4
Band pass: 30–3,000 Hz
Analysis time: 45 ms
Repetitions per average: 500
No. of channels used simultaneously: three
Electrode type: silver-silver chloride
Electrode impedance: <5 K ohm
Electrode placement: Scalp electrodes were placed in accordance with in international 10-20 system and affixed with collodion

Montage Channel	Derivation	Component Measured
1	C3′ or C4′-Fz	$N\overline{20}$
2	C2S-Fz	$N\overline{13}$
3	EP_1-EP_2	EP (Erb's point potential–$N\overline{9}$)

Stimulation and recording parameters for MN-SSEPs followed the American Electroencephalographic Society guidelines[8] and are presented in table 2. Either the left or right median nerve was stimulated at the wrist, and recordings were made from electrodes located at Erb's point over the brachial plexus, the spinous process of the second cervical vertebra (C-2S) and the contralateral sensory cortex (C3′ or C4′ of the international 10–20 System). Intensity of stimulation current varied among patients. Each patient's sensory threshold (minimal current the patient could feel) and motor threshold (when movement of thumb was first visible) were determined in preoperative studies. We used a stimulus intensity equal to motor threshold for recording of control traces. Stimulus intensity was increased to twice the motor threshold after induction of anesthesia. The effect of altering stimulus intensity alone was evaluated in three patients in whom MN-SSEPs were recorded with variable stimulus intensity, while end-tidal concentration of isoflurane and other variables were held constant. At least two averages were obtained for each recording to assure reproducibility, and a mean of two readings was used for measurement of peak latencies and amplitude of Erb's point potential (EP), cervical potential ($N\overline{13}$), and scalp potential ($N\overline{20}$). From these values conduction times EP-$N\overline{13}$; $N\overline{13}$-$N\overline{20}$, and EP-$N\overline{20}$ were calculated.

STATISTICAL ANALYSIS

Mean and standard deviation of values for various peak latencies, conduction times, and amplitude were calculated. Numerical data were subjected to repeated-measures analysis of variance using Hotelling's T-square test[9] to determine statistical significance. A P value less than 0.05 was considered significant. This statistical approach is most appropriate for studies involving repeated measurements in the same individual at different times but its disadvantage is that it is applicable only to a data set in which all measurements have been made at all time

points. Because it was not possible to administer all concentrations of isoflurane to all patients, values obtained in 13 patients that could be studied at both 1.0% and 1.5% end-tidal isoflurane concentrations were included for repeated-measures analysis of variance.

Results

Satisfactory traces were obtained in all patients studied. All patients were hemodynamically stable, and mean arterial pressure was within 15% of control readings. Maximum esophageal temperature change during the study period was 0.5° C. Figure 1 shows a typical trace, along with identification of various components of MN-SSEPs for measurement of peak latencies and calculation of conduction times. Amplitude was measured from each identified negative peak to the next positive peak. The effect of isoflurane on morphology of various MN-SSEPs of a representative patient is shown in figure 2. EP and N$\overline{13}$ peaks remained well defined and without significant increase in their peak latencies. Contralateral scalp responses (N$\overline{20}$) were reduced in amplitude but were evident in all patients after end-tidal concentrations of 0.5 and 1.0%; in 13 out of 14 patients after 1.5%; and in seven out of ten patients after 2% isoflurane. N$\overline{20}$ latency and conduction time EP-N$\overline{20}$ progressively increased with increasing concentration of isoflurane. Mean increase in latency of N$\overline{20}$ in seven patients after 2% isoflurane was 3.7 ms, the range being 2.1–5.0 ms. Mean EP-N$\overline{20}$ conduction time increased by 3.2 ms, with a range of 1.7–4.4 ms. MN-SSEPS components later than N$\overline{20}$ were less durable and could not be identified after administration of 0.5% isoflurane.

Mean values for latencies of different peaks at various end-tidal concentrations studied are shown in table 3. Peak latencies of EP, N$\overline{13}$, and N$\overline{20}$ recorded after 1% and 1.5% isoflurane increased significantly when compared with control values. The difference between latencies of EP and N$\overline{13}$ after administration of 1% and 1.5% isoflurane was not significant (not dose-related), while that for latency of N$\overline{20}$ was significant. Numerical values for conduction times of MN-SSEPS are shown in table 4. There

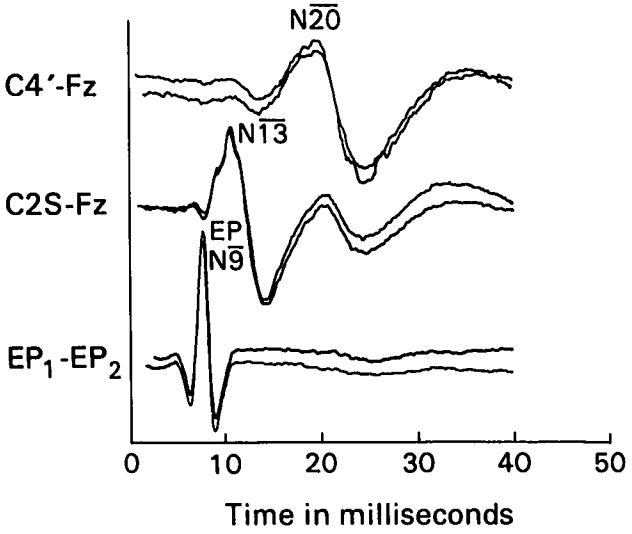

FIG. 1. Typical traces of MN-SSEPs. The points at which measurements of absolute latency of different evoked potentials were made in each derivation have been identified. Negative waveforms in this and other figures are represented by an upward deflection.

was no significant change in conduction time EP-N$\overline{13}$ with 1% or 1.5% isoflurane, while conduction time N$\overline{13}$-N$\overline{20}$ increased significantly compared with control values. N$\overline{13}$-N$\overline{20}$ conduction times recorded at 1% and 1.5% concentrations of isoflurane also differed significantly. Similarly, EP-N$\overline{20}$ conduction time increased significantly after administration of isoflurane when compared with control values, and the difference between 1% and 1.5% isoflurane was also significant. Table 5 shows the numerical values for amplitude of different components of MN-SSEPs. There was no significant change in amplitude of EP and N$\overline{13}$ with 1% or 1.5% isoflurane compared with control values, nor was the difference between two concentrations significant. By contrast there was a remarkable reduction of amplitude of N$\overline{20}$ with isoflurane anesthesia compared with control values, and a difference between 1% and 1.5% isoflurane was statistically significant. There was further decrease in amplitude of N$\overline{20}$ after 2% isoflurane. We wish to emphasize that the effect of isoflurane on amplitude of N$\overline{20}$ was highly variable and as already

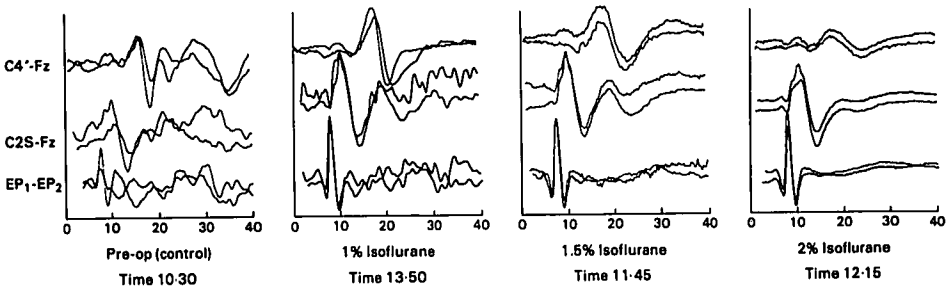

FIG. 2. Left median nerve SSEP monitoring with isoflurane anesthesia. The effect of different concentrations of isoflurane in one representative patient is shown. EP (EP_1-EP_2 derivation) and N$\overline{13}$ (C2S-Fz derivation) show lack of change in latency and morphology, while change in amplitude of N$\overline{20}$ (C4'-Fz derivation) with increase in end-tidal isoflurane from 1% to 2% is obvious.

TABLE 3. Latencies (mean ± SD) of Different Peaks of MN-SSEPs at Different Concentrations of Isoflurane

End-tidal Isoflurane (volume %)	EP		N$\overline{13}$		N$\overline{20}$	
	N	Value (ms)	N	Value (ms)	N	Value (ms)
Control	13	10.28 ± 0.75*	13	13.93 ± 0.90*	13	19.45 ± 1.46*
0.5	7	11.21 ± 0.98	7	14.77 ± 1.89	7	21.66 ± 1.95
1.0	13	10.90 ± 0.77*	13	14.65 ± 1.45*	13	22.21 ± 2.09*
1.5	13	10.80 ± 0.74*	13	14.57 ± 1.35*	13	22.94 ± 1.71*
2.0	10	10.32 ± 0.74	10	14.26 ± 1.26	7	22.85 ± 1.71*
P value	13	0.0003	13	0.0356	13	0.0000
Pairwise Comparisons						
Control *vs.* 1		Significant		Significant		Significant
Control *vs.* 1.5		Significant		Significant		Significant
1 *vs.* 1.5		NS		NS		Significant

NS = not significant.

* Values included in repeated measures analysis of variance.

mentioned, in three out of ten patients studied with 2% isoflurane, N$\overline{20}$ could not be identified. We noted that the predominant effect of change in stimulus intensity (in three patients studied) was a change in amplitude with minimal change in latency (fig. 3). A slight change in latency can be attributed to a better description of an individual component, which allows more precise measurement of latency.

Discussion

The objectives of this study were to: 1) determine if MN-SSEPs can be successfully recorded in patients anesthetized with isoflurane; 2) quantitate the effect of isoflurane on change in latency and amplitude of MN-SSEPs; and 3) compare the effect of isoflurane on MN-SSEPs with different neural generators, thereby studying the differential effects of isoflurane on different parts of the nervous system.

Our patients were free of neurologic disease, with the exception of those with lumbar radioculopathy undergoing lumbar laminectomy. All were undergoing surgical procedures that do not have any effect on neural pathways assessed by MN-SSEPs. Anesthesia was maintained with oxygen and isoflurane following induction with thiamylal. Shimoji and co-workers[10] have shown that thiamylal (5 mg/kg) has a significant effect on both scalp and spinal evoked response. However, in their study SSEPs had returned to control values after 8–10 min. In our study the minimum interval between administration of thiamylal and recording of MN-SSEPs was 20 min. Other significant factors to be considered in the design of this study are time-dependent changes and those related to change of technical parameters such as stimulus intensity. Turner and co-workers[11] have, indeed, shown significant time-dependent changes in cerebral and cardiovascular parameters in dogs anesthetized with isoflurane and nitrous oxide. Their study showed significant cerebral vasodilation with isoflurane–nitrous oxide anesthetic, but this effect diminished with time. The order of different concentrations of isoflurane in our patients was varied (table 1) to nullify any effect that duration of anesthesia alone might have had. We observed similar effects of anesthetic concentration (0.5% and 1.5%) in five individual patients, regardless of whether MN-SSEPs were recorded at the beginning or toward the end of 3–4 h of anesthesia.

TABLE 4. Conduction Times (mean ± SD) of MN-SSEPs at Different Concentrations of Isoflurane

End-tidal Isoflurane (volume %)	EP-N$\overline{13}$		N$\overline{13}$-N$\overline{20}$		EP-N$\overline{20}$	
	N	Value (ms)	N	Value (ms)	N	Value (ms)
Control	13	3.65 ± 0.40*	13	5.52 ± 1.13*	13	9.17 ± 1.08*
0.5	7	3.56 ± 1.46	7	6.89 ± 1.30	7	10.45 ± 2.00
1.0	13	3.75 ± 0.76*	13	7.56 ± 1.68*	13	11.31 ± 1.71*
1.5	13	3.77 ± 0.72*	13	8.37 ± 1.49*	13	12.14 ± 1.56*
2.0	10	3.94 ± 0.74	7	9.01 ± 0.73	7	12.68 ± 0.58
P value	13	0.73	13	0.0000	13	0.000
Pairwise Comparisons						
Control *vs.* 1		NS		Significant		Significant
Control *vs.* 1.5		NS		Significant		Significant
1 *vs.* 1.5		NS		Significant		Significant

NS = not significant.

* Values included for repeated measures analysis of variance.

TABLE 5. Amplitude (mean ± SD) of Different Peaks of MN-SSEPs at Different Concentrations of Isoflurane

End-tidal Isoflurane (volume %)	EP		N$\overline{13}$		N$\overline{20}$	
	N	Value (μvolt)	N	Value (μvolt)	N	Value (μvolt)
Control	13	2.49 ± 1.50	13	2.34 ± 0.75	13	3.07 ± 2.00
0.5	7	2.67 ± 1.05	7	2.38 ± 0.72	7	1.50 ± 0.84
1.0	13	2.28 ± 1.64	13	2.19 ± 0.91	13	1.54 ± 1.06
1.5	13	2.19 ± 1.67	13	2.16 ± 0.84	13	1.07 ± 0.78
2.0	10	2.44 ± 1.78	10	2.00 ± 0.93	7	0.96 ± 0.63
P value		.59		0.65		0.0009
Pairwise Comparisons						
Control *vs.* 1		NS		NS		Significant
Control *vs.* 1.5		NS		NS		Significant
1 *vs.* 1.5		NS		NS		Significant

NS = not significant.

Despite the increased use of SSEPs for intraoperative monitoring, there are no definite criteria regarding choice of stimulus intensity that should be used for the recording of SSEPs during surgery.[8] Most laboratories use stimulus intensities of either motor threshold or just above motor threshold. The study of McPherson *et al.*[7] of anesthetics on SSEPs used stimulus intensity of motor threshold in unanesthetized patients and arbitrarily increased it to three times the motor threshold in anesthetized patients. Drummond *et al.*[12] used stimulus intensity of motor threshold +20%. However, the effect of stimulus intensity alone on somatosensory evoked potentials has been previously investigated in detail in unanesthetized patients.[13-15] Lesser and co-workers[13] reported that in awake volunteers, motor threshold stimulation gave consistently submaximal responses, while a sum of motor plus sensory threshold gave potentials that were consistently close to maximal amplitude; and when stimulus intensity was increased, no remarkable change was seen in absolute latency of N$\overline{9}$ and N$\overline{18}$, while latency of N$\overline{13}$ decreased slightly. Nuwer and Dawson,[14] while studying the effects of different stimulation and recording parameters on SSEPs in anesthetized patients, reported that as stimulus intensity was gradually increased, the amplitude of SSEPs increased to reach a plateau at about 20 milliamperes. They did not comment on any change in latency. Tsuji *et al.*[15] have studied the effect of stimulus intensity on subcortical and cortical evoked potentials after stimulation of posterior tibial nerve. They have recommended the use of stimulus intensity three times the sensory threshold. We felt that use of such a strong stimulation current (while awake) was not justified in our volunteer patients in whom this monitoring was not medically indicated. Therefore, like previous investigators, we recorded MN-SSEPs with stronger current after induction of anesthesia. We noted that the predominant effect of change in stimulation intensity was a change in amplitude with a minimal change in latency (fig. 3). Therefore, some of the effect of isoflurane on amplitude of MN-SSEPs in our study as well as previously published studies might have been counterbalanced by change in stimulus intensity.

Our results show that latencies of all measured components (EP, N$\overline{13}$, and N$\overline{20}$) increased significantly after isoflurane (1% and 1.5%) when compared with control values. A comparison between recordings made after 1% isoflurane and 1.5% isoflurane shows no significant difference between peak latencies of EP and N$\overline{13}$, while latency of N$\overline{20}$ shows a significant difference. Two explanations for these observations are: 1) this difference in increase in latency of various peaks with different generator sources represents differential effects of isoflurane at different parts of nervous systems; or 2) an increase in peak latencies of EP and N$\overline{13}$ does not represent an effect

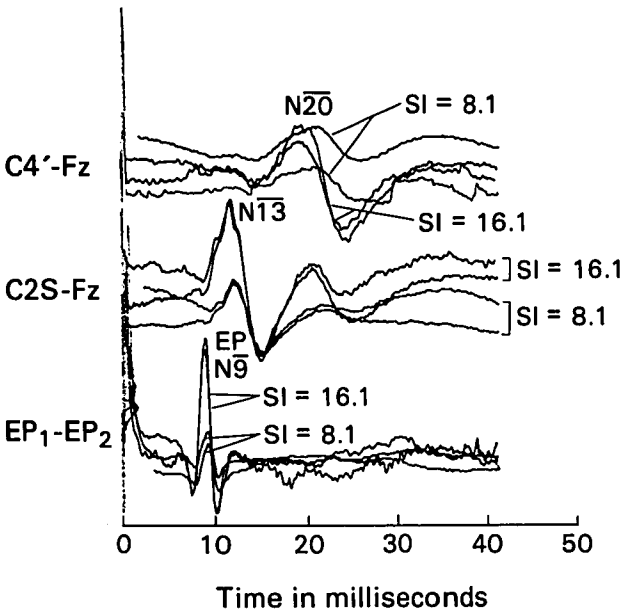

FIG. 3. Effect of stimulus intensity (SI) on MN-SSEPs in one patient anesthetized with isoflurane (1.5% end tidal). All recordings were made in duplicate to document reproducibility. Increase in stimulus intensity resulted in increase in amplitude without significant change in latency of various MN-SSEPs components.

of isoflurane because it is not dose related, but is due to other physiologic and/or technical variables. Physiologic variables that are known to affect sensory evoked potentials (hemodynamic stability, Pa_{CO_2}, and temperature) were carefully controlled in this study. While the maximum decrease in esophageal temperature noted was 0.5° C, changes of temperature of the upper limb itself might have contributed to slight increases in latency of EP. Positioning of the upper limb, which was outstretched during surgery, could also have accounted for minor increases of peak latencies. Conduction times are independent of both limb position and limb temperature. Conduction time EP-N$\overline{13}$ did not change significantly with 1% and 1.5% isoflurane when compared with control values. Conduction time N$\overline{13}$-N$\overline{20}$ increase significantly with isoflurane when compared with control values, and the difference in values with 1% and 1.5% isoflurane was also statistically significant. The total conduction time EP-N$\overline{20}$ showed similar changes because N$\overline{13}$-N$\overline{20}$ conduction is a major contributor to this measurement. These data suggest that isoflurane has differential effects on the human nervous system.

Generator sources of median nerve evoked potentials have been postulated based on animal, clinical, and clinicopathologic studies. The state of present knowledge on this subject has been critically examined by Emerson and Pedley,[16] who concluded that EP is the afferent volley in the brachial plexus at the Erb's point. N$\overline{13}$ is a postsynaptic potential recorded maximally near the cervicomedullary junction, with near and far field components. Its generator is probably dorsal gray matter of the rostral cervicel spinal cord or nucleus cuneatus. N$\overline{20}$ is probably the first cortical response to sensory input that may have more than one generator. No significant change in EP-N$\overline{13}$ conduction time and a significant change in N$\overline{13}$-N$\overline{20}$ conduction time in our study suggests a greater impairment of synaptic transmission compared with afferent fiber conduction by isoflurane. This mechanism explains the difference in isoflurane's effect on amplitude of various components of MN-SSEPs. EP and N$\overline{13}$, with generator sources in peripheral nerve and spinal cord, do not involve multiple synapses, and their amplitude is not affected by increasing concentrations of isoflurane. By contrast N$\overline{20}$ with its postulated generator source in thalamocortical radiation or sensory cortex involves multiple synapses and shows progressive decrease in amplitude with increasing concentrations of isoflurane. Similar differential effects with thiamylal[10] in humans and other depressant drugs and intravenous anesthestics[17] in cats have been previously reported.

Our findings contradict the report of Nuwer and Dawson.[14] Their study reported four patients in whom MN-SSEPs were being monitored while isoflurane was used in an unreported concentration. Three out of four patients demonstrated no recordable MN-SSEPs after 20 min of isoflurane, while in one patient, small EP could be seen at 0.5% isoflurane. This was abolished when anesthetic concentration was raised to 0.75%. We obtained satisfactory traces in all patients receiving 0.5 and 1% and in 13 out of 14 patients who received up to 1.5% isoflurane. N$\overline{20}$ could not be identified in only three out of ten patients after 2% isoflurane. One possible explanation for this difference may be that their patients received nitrous oxide and narcotics in addition to isoflurane. Nitrous oxide alone[18] and in the presence of narcotics has been shown to decrease the amplitude of MN-SSEPs. Two other recent studies[7,19] have reported an effect of isoflurane on MN-SSEPs. McPherson and co-workers[7] have compared the effect of administration of small concentrations (0.25–1%) of isoflurane with nitrous oxide (50%) on the cortical (N$\overline{20}$) component of median nerve evoked potentials in patients anesthetized with thiopental (varying doses) and fentanyl (25 μg/kg). They reported a greater decrease in amplitude of N$\overline{20}$ with nitrous oxide than isoflurane and an increase in latency with isoflurane, but not nitrous oxide. They concluded that supplementation of anesthesia with isoflurane may be preferable to that with nitrous oxide in patients having intraoperative monitoring of MN-SSEPs under fentanyl anesthesia. Our results are in agreement with their findings that MN-SSEPs can be successfully recorded in patients anesthetized with isoflurane. McPherson's study did not provide data on the effect of isoflurane on MN-SSEPs because the design of their study was such that their patients received variable concentrations of isoflurane, end-tidal concentration of isoflurane at the time of recording of SSEPs was not monitored, and their patients received variable amounts of intravenous anesthetics. More recently Peterson and co-workers[19] have studied the effects of halothane, enflurane, isoflurane, and nitrous oxide on MN-SSEPs. They successfully recorded MN-SSEPs in patients anesthetized with 0.5, 1, and 1.5 MAC isoflurane and 60% nitrous oxide and reported a progressive increase in latency and a decrease in amplitude of cortical (N$\overline{20}$) component along with an increase in central (N$\overline{13}$-N$\overline{20}$) conduction time. Our results with low concentrations (0.5% and 1%) of isoflurane are in agreement with their findings. However, we successfully recorded MN-SSEPs at 1.5% isoflurane in 13 out of 14 patients, while in five of seven patients, Peterson *et al.* failed to record a discernible N$\overline{20}$ response at 1.5 MAC of isoflurane. In our study, we also failed to identify N$\overline{20}$ in 30% patients with 2% (end-tidal) isoflurane. Two possible explanations for this difference are that: 1) In the study of Peterson *et al.* addition of nitrous oxide might have contributed to the effect of isoflurane. Sebel *et al.*[18] have shown that inhalation of 50% nitrous oxide by awake volunteers resulted in nearly 45% reduction of amplitude of N$\overline{20}$. 2) Marked attenuation of the cortical component

may be occurring between 1.5 and 2% isoflurane concentrations; hence, at 1.5 MAC (1.74%) in their study they failed to record N$\overline{20}$ potential in a majority of their patients.

Our data suggest that conduction times provide a better measure of effects of anesthetics on SSEPs than peak latencies. Upper limb positioning alone can alter the peak latency of EP, which contributes to an increase in peak latencies of N$\overline{13}$ and N$\overline{20}$. Conduction times EP-N$\overline{13}$ and N$\overline{13}$-N$\overline{20}$ are independent of position of the limb during surgery. Subcortical potentials like N$\overline{13}$ are less affected by isoflurane than cortical potentials. Therefore, in procedures involving cervical spinal cord, intraoperative monitoring of SSEPs is possible even with high isoflurane concentrations as N$\overline{13}$ can be reliably monitored. In procedures placing brain stem or cerebral somatosensory pathways at risk, the N$\overline{20}$ potential would be the appropriate component to be monitored, and this can be accomplished in most cases at lower isoflurane concentrations. N$\overline{20}$ may be lost in many cases at higher concentrations; therefore, concentrations above 1.5% isoflurane should be avoided.

An increase in latency and a decrease in amplitude of cortical components of somatosensory evoked potentials after stimulation of median and posterior tibial nerves with fentanyl and morphine anesthesia has been reported.[5,20] Despite the changes in latency and amplitude, cortical potentials could be identified in all patients anesthetized with fentanyl. Therefore, use of narcotic anesthesia is preferable in patients in whom SSEPs are being monitored. But use of high-dose narcotics has the drawback of ventilatory depression in the postoperative period and may not be the ideal technique in some patients. In that group of patients use of isoflurane in concentrations up to 1–1.5% is feasible. Differences in stimulation and recording parameters used by different investigators make a comparison of effects of inhalation and intravenous anesthetics on SSEPs difficult. It seems that a comparative study of effects of inhalation and intravenous anesthetics is warranted before a strong recommendation to use one group of drugs *versus* the other can be made. It is also possible that the effect on latency and amplitude of various components of SSEPs may be a reflection of depth of anesthesia rather than the specific anesthetic used. Therefore, simultaneous monitoring of the electroencephalogram to assure equal depth of anesthesia will make the comparative study of different anesthetics on SSEPs more meaningful.

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