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Median nerve somatosensory evoked potentials during isoflurane anaesthesia

Purpose: The effect of isoflurane on the subcortical P_{14} component of the median nerve somatosensory evoked potential (SEP) is poorly known. We studied whether the P_{14} wave from the upper brainstem, recorded with a nasopharyngeal electrode, was attenuated at the isoflurane-induced EEG burst-suppression level. We also compared the effect of isoflurane on the P_{14} , cervical N_{13} and cortical N_{20} , N_{35} and N_{60} components.

Methods: Seventeen elective patients were anaesthetized with isoflurane. Somatosensory evoked potentials were recorded prior to anaesthesia, at 0.5 MAC and 1 MAC end-tidal isoflurane as well as at the level when EEG was in burst-suppression (mean 1.9 vol% end-tidal isoflurane).

Results: Isoflurane had varying effects on the subcortical components of median SEP. The amplitude of nasopharyngeal P_{14} was stable, but the mean latency increased from 14.4 ± 1.2 msec at 0.5 MAC to 15.2 ± 1.1 msec at burst-suppression level ($P < 0.05$). In contrast, the N_{13} neck response amplitude was attenuated from 3.3 ± 0.6 μ V to 2.6 ± 0.5 μ V ($P < 0.005$) without latency changes. The latency of the cortical N_{20} wave was increased from 19.7 ± 1.1 msec at awake to 24.4 ± 1.6 msec at burst-suppression level ($P < 0.0001$) and amplitude was reduced from 3.3 ± 1.1 μ V to 1.3 ± 0.6 μ V ($P < 0.0001$). The later cortical components were attenuated even during 0.5 MAC isoflurane and were not recordable during EEG burst-suppression.

Conclusion: We conclude that P_{14} can reliably be recorded with nasopharyngeal electrodes during isoflurane anaesthesia, even during EEG burst-suppression, when the N_{20} wave is attenuated. In contrast, the middle-latency SEP components are sensitive to isoflurane anaesthesia.

Objectif : Nous connaissons mal l'action de l'isoflurane sur la composante sous-corticale P_{14} du potentiel somatosensoriel évoqué (SEP) du nerf médian. Nous avons cherché si l'onde P_{14} enregistrée à la partie supérieure du tronc cérébral avec une électrode nasopharyngée diminuait lorsque l'isoflurane ralentissait l'EEG jusqu'au niveau *burst-suppression*. Nous avons aussi comparé l'influence de l'isoflurane sur les composantes P_{14} , cervicale N_{13} et corticales N_{20} , N_{25} et N_{60} .

Méthodes : Dix-sept patients électifs ont été anesthésiés à l'isoflurane. Les potentiels évoqués somatosensoriels ont été enregistrés avant l'anesthésie, à 0,5 MAC et à 1,0 MAC télé-expiratoires et au niveau de *burst-suppression* EEG (concentration télé-expiratoire 1,9% d'isoflurane).

Résultats : L'isoflurane avait des effets variés sur les composantes non-corticales des SEP médians. L'amplitude du P_{14} nasopharyngé était stable, mais la latence moyenne augmentait de $14,4 \pm 1,2$ ms à 0,5 MAC à $15 \pm 1,1$ ms pendant le *burst-suppression* ($P < 0,05$). Par contre, l'amplitude de la réponse N_{13} cervicale était atténuée de $3,3 \pm 0,6$ μ V à $2,6 \pm 0,5$ μ V ($P < 0,005$) avec une latence inchangée. La latence de l'onde corticale N_{20} augmentait de $19,7 \pm 1,1$ ms à l'état vigile à $24,4 \pm 1,6$ ms pendant le *burst-suppression* ($P < 0,0001$). Les dernières composantes corticales diminuaient même sous isoflurane 0,5 MAC et n'étaient pas enregistrables pendant le *burst-suppression* à l'EEG.

Conclusion : Nous concluons qu'il est possible d'enregistrer P_{14} fidèlement avec des électrode nasopharyngées pendant l'anesthésie à l'isoflurane, même pendant le *burst-suppression* lorsque l'onde N_{20} est atténuée. Par contre, les composantes SEP de latence moyenne sont sensibles à l'anesthésie à l'isoflurane.

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SOMATOSENSORY evoked potentials (SEPs) to median nerve stimulation can be recorded during anaesthesia to monitor the sensory pathways during different surgical procedures.¹ Recently, the generators of different subcortical waves of the SEP have been studied in normal subjects as well as in patients with well-defined neurological deficits.^{2,3} It has been shown that recording from an electrode in the nasopharynx can help to distinguish the electrical activity generated by the spinal cord below the foramen from the subcortical activity above the foramen, both generating approximately 13–14 msec after electrical stimulus at the wrist, and this could be used in evaluation of cervical damage and brain death.⁴

While the effects of different anaesthetics on somatosensory evoked potentials have been extensively investigated,^{5–10} no studies have been published on the subcortical components separated with the nasopharyngeal electrode during anaesthesia. As isoflurane is known to attenuate the cortical components of SEP,^{7,9–11} but is often a useful anaesthetic in neurosurgery, we decided to study whether it affects the subcortical components.

The N₂₀ wave of the SEP, probably generated at the posterior edge of the central sulcus, can be represented by a dipole parallel with the scalp.¹² This dipole produces a positive deflection in front and a negative behind. Isoflurane attenuates the N₂₀; nevertheless, in some patients it can be recorded during continuous EEG suppression.¹¹

The cortical components following the N₂₀ are variable and their generators less well known.^{13–15} However, the components following N₂₀ up to 100 msec have been claimed to be more sensitive to ischaemia than the earlier waves, and it has been suggested that monitoring them should be useful during anaesthesia.^{16,17} They are, however, highly sensitive to anaesthetics.^{18,19} We sought here to compare them with the subcortical components as well as with the N₂₀ during isoflurane.

Methods

The protocol was approved by the Hospital Ethics Committee, and patients gave their informed consent. Seventeen ASA I–II patients (eleven male, six female) participated in the study. The mean age of the patients was 34.1 yr, range 18–46 yr. Their mean weight was 71 ± 11.3 kg, and mean height 174 ± 9.0 cm. No patient showed evidence of neurological disease or used medication affecting the central nervous system. Operations consisted of abdominal, orthopaedic and mammary gland surgery.

Oxazepam (0.3–0.5 mg·kg⁻¹) was given *po* as premedication about one hour before anaesthesia. Anaesthesia

was induced by mask with isoflurane in nitrous oxide/oxygen. Prior to induction, 0.2 mg glycopyrrolate was given *iv*. Succinylcholine 75 mg was used to facilitate orotracheal intubation, and 0.1 mg·kg⁻¹ vecuronium for neuromuscular block. Additional doses of vecuronium were given guided by train-of-four stimulation.

After induction of anaesthesia, nitrous oxide was discontinued and anaesthesia was continued with isoflurane in air/oxygen (FiO₂ 0.4). Normocapnia (end tidal carbon dioxide 4.5–6.0 kPa) was maintained. Arterial pressure was measured noninvasively at three minute intervals. The end tidal isoflurane concentration was monitored continuously by a Datex Normac^R (Datex, Finland) anaesthetic agent monitor. Temperature was monitored from the nasopharynx and from the dorsum of the stimulated arm, and body cooling was prevented by warmed infusion fluids and a heating blanket.

Somatosensory evoked potentials to median nerve stimulation were recorded with a Neuropack Four Mini^R (Nihon Kohden, Japan) evoked potential analyser. The median nerve was stimulated at the wrist with a surface electrode. The motor threshold was sought before anaesthesia and during anaesthesia the stimulus intensity was doubled. The pulse width was 0.2 msec and the stimulation frequency 4 Hz. The AD sampling rate for subcortical responses was 10000 samples·sec⁻¹ (analysis time 50 msec) and for cortical responses 2500 samples·sec⁻¹ (analysis time 200 msec). Automatic artefact rejection was used.

The N₉ component of the brachial plexus was recorded from Erb's point, referred to the contralateral Erb's point. The N₁₃ wave was recorded from an electrode on the spine of the 7th cervical vertebra, referred to the forehead. The P₁₄ was recorded from a nasopharyngeal electrode (Pg_z), referred to the forehead. The scalp SEP was from C3' or C4' (International 10–20 system), referred to the forehead. Scalp electrodes were platinum needles, the nasopharyngeal electrode was an insulated silver wire with a ball tip. This was inserted after induction of anaesthesia. Ag/AgCl surface electrodes were used at other locations. Electrode impedances were < 5 kOhm. The recording band width was 2–500 Hz for scalp SEP and 20–3000 Hz for other channels.

Two hundred sweeps, repeated two to three times for each patient were averaged at each recording condition. The averaged curves were summed to form a grand average for every patient which was used to determine latencies and amplitudes at each stage.

The first SEPs were recorded in the operating theatre immediately before the induction of anaesthesia. After induction, the isoflurane concentration was adjusted to 0.6% end tidal concentration corresponding to 0.5

MAC.²⁰ After 15 min, the second series of SEPs was recorded. Thereafter anaesthesia was deepened to 1.2% end tidal isoflurane (1 MAC) and surgery commenced. Another series of SEPs was recorded after 15 min. Finally, the isoflurane concentration was increased to a point at which a burst-suppression pattern appeared on the EEG, (mean) $1.9 \pm 0.17\%$ end tidal isoflurane and maintained at this level for 15 min before recording the SEPs. Mean arterial pressure (MAP) at this stage was 73 ± 14 mmHg, and average heart rate 98 ± 23 beat·min⁻¹. In four patients anaesthesia was further deepened to a point at which the EEG was in continuous suppression (mean) $2.2 \pm 0.1\%$ end tidal isoflurane, and after five minutes of suppression the last series of SEPs was recorded. The MAP at this stage was 72 ± 17 mmHg, and average heart rate 90 ± 23 beat·min⁻¹.

Statistical analysis

Analysis of variance for repeated measurements was used for SEP changes. The data are given as means $\pm$ SD. Oesophageal temperature was used as a covariate to discount the effects of minor temperature changes during the study.

Results

The subcortical P₁₄ and cortical N₂₀ SEP responses are shown in one patient (Figure 1) during different stages of isoflurane anaesthesia. The mean latencies and amplitudes of N₁₃ and P₁₄ are presented in Table I. The P₁₄ wave was consistently recorded during different levels of isoflurane anaesthesia, except in one recording, in which the P₁₄ at 0.5 MAC showed poor quality due to technical artefacts. This missing value was replaced by the mean value of the rest of the patients in the statistical analysis, and the degrees of freedom were correspondingly adjusted.

We recorded the P₁₄ with Fz-Pgz derivation, in which the P₁₄ appears as a positive, downward deflec-

FIGURE 1 Somatosensory evoked potentials in one patient at 0.5 MAC, 1 MAC, EEG burst-suppression level (B-S) and at the level where EEG was continuously suppressed (S). Upper curve: P₁₄ and P₂₀ recorded from scalp electrode (Fz) and nasopharyngeal electrode (PgZ). The first downward peak is P₁₄, the second larger peak is P₂₀ (positive counterpart of N₂₀). Positive at Fz is downwards. Lower curve: N₂₀ recorded from C'3 or C'4 electrode and Fz, negative at C'3 or C'4 is upwards. P₁₄ amplitude is stable with rising concentrations of isoflurane, and its distance from P₂₀ increases corresponding to the increase in P₂₀ latency. The N₂₀ wave, decreases in amplitude with increasing isoflurane concentration. Vertical lines indicate stimulation time points and 20 msec thereafter.

tion. The other positive deflection following P₁₄ in Figure 1 is probably that generated by the dipole generating the N₂₀/P₂₀, and possibly represents simultaneous activity of the P₂₂ generator.

The latencies of both N₁₃ and P₁₄ increased when the isoflurane concentration was increased, but only the P₁₄ latency shift was significant ($P < 0.05$). A more precise analysis showed this difference to be at the burst-suppression level between the P₁₄ and the N₁₃.

The amplitude of P₁₄ was stable with increasing isoflurane concentration, while that of N₁₃ decreased from 3.3 ± 0.6 μ V to 2.6 ± 0.5 μ V ($P < 0.005$) between 0.5 MAC and burst-suppression level. With the four patients whose anaesthesia was deepened to the point of EEG suppression, the latency of N₁₃ or P₁₄ did not increase, but the amplitude of both decreased.

TABLE I Subcortical components of median nerve SEP during isoflurane anaesthesia.

	awake	0.5 MAC	1 MAC latency (msec)	BS	S(n=4)
N ₁₃	13.7 ± 0.9	14.0 ± 1.1	14.1 ± 1.2	14.4 ± 1.2	14.1 ± 0.9
P ₁₄	—	14.4 ± 1.2	14.7 ± 1.3	15.2 ± 1.1 ns $P < 0.05$	15.3 ± 1.4
			amplitude (μ V)		
N ₁₃	3.3 ± 0.8	3.3 ± 0.6	2.8 ± 0.5	2.6 ± 0.5 $P < 0.005$	2.4 ± 0.2
P ₁₄	—	1.0 ± 0.3	1.0 ± 0.3	1.0 ± 0.4 ns	0.8 ± 0.2

Values are means $\pm$ SD. BS = burst-suppression of the EEG. S = suppression of the EEG. A repeated ANOVA between 0.5 MAC and burst-suppression levels.

FIGURE 2 Cortical SEP components in one patient during isoflurane anaesthesia. The components following the N_{20} wave are attenuated and their latencies increased even at a 0.5 MAC level of isoflurane anaesthesia. Above 1 MAC the only remaining wave is N_{20} . Vertical lines indicate stimulation time point and 50 msec thereafter. B-S = burst-suppression of the EEG, S = suppression of the EEG. Negative upwards.

The primary cortical N_{20} wave was recorded at a mean latency of 19.7 ± 1.1 msec before anaesthesia. Following the N_{20} , a second negative cortical wave N_{35} , which appeared at a mean peak latency of 35 ± 3.0 msec, was identified in all patients. Finally, an N_{60} wave was seen in 16 of 17 patients before anaesthesia, with a mean latency of 57.8 ± 8.6 msec. The cortical SEP components in one representative patient before induction of anaesthesia and during different isoflurane concentrations are shown in Figure 2.

Table II presents the cortical components, their latencies and amplitudes at different levels of isoflurane anaesthesia. The N_{20} component was recordable from 0.5 MAC to burst-suppression level in 16 of 17 patients. At 0.5 MAC, a delayed N_{35} was seen in all patients, but only 11 had the N_{60} response, reduced in amplitude and with an increased latency. At 1 MAC, none of the patients had the N_{60} wave and the N_{35} was seen in only eight cases.

During burst-suppression and suppression no middle-latency responses were seen, and the amplitude of N_{20} was attenuated.

Discussion

The results of the present study indicate that the subcortical P_{14} wave to median nerve stimulation recorded from the nasopharynx is stable during isoflurane anaesthesia. The amplitude of P_{14} was not affected by increasing isoflurane concentration from 0.5 MAC to 1.6 MAC (burst-suppression level). The latency of P_{14} increased by 0.9 msec on the average; however, this latency shift must be interpreted as clinically insignificant. Among the patients, the largest individual increase in P_{14} latency was 18% between 0.5 MAC and burst-suppression, and the maximum amplitude decrease was 49%. We consider these changes to be caused by isoflurane and, therefore, latency or amplitude alterations outside these limits could be interpreted as pathological.

The effect of isoflurane on P_{14} has been previously studied only by Vandestein *et al.*⁷ They reported no change in P_{14} latency, but they did not study isoflurane concentrations as high as in the present study. Furthermore, they did not use nasopharyngeal electrodes, and the reference for P_{14} was a linked earlobe instead of the forehead. Some difficulties in recording P_{14} reliably were also reported, and the amplitudes were therefore not reported. The nasopharyngeal recording in the present study produced good quality responses P_{14} being readily seen in different concentrations of isoflurane.

The P_{14} wave, originally defined from scalp recording with noncephalic reference, is claimed to be gener-

TABLE II The cortical SEP responses to median nerve stimulation during isoflurane anaesthesia.

	awake	0.5 MAC	1 MAC latency (msec)	BS	S (n=4)
N_{20}	19.7 ± 1.1	22.6 ± 2.3	22.7 ± 1.3	24.4 ± 1.6 $P < 0.0001$	24.5 ± 1.8
N_{35}	34.5 ± 3.0	54.2 ± 26.3 $P < 0.01$	69.2 ± 19.3 $n=8$	—	—
N_{60}	57.8 ± 8.6 $n=16$	105.5 ± 18.4 $n=11$	—	—	—
			amplitude (μV)		
N_{20}	3.3 ± 1.1	2.4 ± 1.7	1.8 ± 1.4	1.3 ± 0.6 $P < 0.0001$	0.9 ± 0.4
N_{35}	3.0 ± 1.4	2.1 ± 1.6 $P: ns$	1.2 ± 0.8 $n=8$	—	—
N_{60}	3.5 ± 1.8 $n=16$	1.8 ± 0.8 $n=11$	—	—	—

Data are presented as means $\pm$ SD. BS = burst-suppression of the EEG. S = suppression of the EEG. A repeated ANOVA between awake and burst-suppression levels for N_{20} component and between awake and 0.5 MAC levels for N_{35} component.

ated in the medial lemniscus.²¹ According to Wagner⁴ the P₁₄ potential involves at least two generators. It has been suggested that monitoring the P₁₄ potential is useful during neurosurgical operations involving the brain stem and craniocervical junction and cervical spine, when the separation of different subcortical potentials generated above and below the foramen magnum is essential.^{22,23} Patients suffering from deep coma due to massive trauma are often given drug therapy to reduce intracranial pressure and the effect of these drugs on different SEP components must then be considered. Further studies are needed to be certain if the P₁₄ wave is preserved similarly with different sedative drugs, as with isoflurane.

Interestingly, the latency of N₁₃ was constant during isoflurane anaesthesia, but the amplitude decreased, in contrast to P₁₄. N₁₃ is a postsynaptic potential generated in the spinal cord gray matter, and the postsynaptic origin of N₁₃ could explain the amplitude decrease during isoflurane. In contrast, the stability of P₁₄ matches the relative insensitivity of far-field potentials to volatile anaesthetics.²⁴

This study confirms earlier reports on the effect of isoflurane on cortical somatosensory evoked potentials which have shown a decrease in the amplitude and an increase in the latency of the waves generated approximately 20 msec and later after stimulation at the wrist.^{7,9-11,25} In the present study the mean latency increase in N₂₀ during isoflurane was 1.8 msec. The SEP components after the N₂₀ are known to be sensitive to several factors, including age,²⁶ vigilance,²⁷ temperature²⁸ and drugs.²⁹⁻³¹ Benzodiazepines have been reported to produce a latency shift in middle-latency SEP components.^{29,32} Barbiturates at doses high enough to cause burst-suppression of the EEG abolish the long-latency components.³³ The results of the present study show that the middle-latency components are highly sensitive to isoflurane concentrations exceeding 0.5 MAC.

The waves after N₂₀ are sensitive indicators of ischaemia and could be used for the monitoring of threatening cerebral ischaemia.^{16,17} However, their sensitivity to isoflurane concentration means that if these waveforms are used in intraoperative monitoring, the isoflurane concentration must be carefully controlled and the responses from the contralateral median nerve stimulation used as control. Nevertheless, the N₂₀ wave could be recorded even at isoflurane levels which cause continuous suppression of the EEG, as has previously been demonstrated during isoflurane¹¹ and barbiturate anaesthesia.³⁴

In conclusion, our study shows that the subcortical P₁₄ wave can be reliably recorded with nasopharyngeal electrodes, and its amplitude is constant through a wide

range of isoflurane concentrations, suggesting the use of P₁₄ for monitoring purposes. On the other hand, its latency increases during isoflurane anaesthesia, but less than that of the cortical N₂₀ response. The N₂₀ wave is reduced to a simple monophasic wave in deep isoflurane anaesthesia, showing an increase in latency and a decrease in amplitude. The cortical components following N₂₀ are delayed and attenuated rendering them difficult to use at isoflurane concentrations exceeding 0.5 MAC.

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