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Effects of Isoflurane on Visual Evoked Potentials in Humans

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Monitoring brain integrity has become important when complicated neurosurgical and vascular procedures are performed. Monitoring of visual evoked potentials (VEP) in anesthetized patients is one of these techniques. The VEP is elicited by flashes coming from light-emitting diodes that are mounted on goggles over the patient's closed eyes. The resulting evoked potentials have a prominent positive peak with a latency of approximately 100 ms from the onset of the stimuli. This peak, which is called the P1 or P100, is thought to be generated in the striated and parastriated visual cortex.[1] It is considered to be a sensitive measure of the integrity of the visual pathways.[1–3]

During neurosurgical procedures involving visual pathways, such as transsphenoidal and anterior fossa surgery, the VEP has been used to monitor the function of the visual pathways.[2,3] Several authors have described the effects of anesthetics on VEP.[4–6] Uhl *et al.* showed that the latency of the P1 in the VEP is longer with increasing concentrations of halothane.[5] Burchiel *et al.* noticed an increase of amplitude in the VEP during enflurane anesthesia.[6] Because isoflurane is often used for neurosurgery, we decided to investigate the effects of isoflurane on the VEP in humans.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board. Twelve patients in ASA Physical Status I and II undergoing elective, nonneurosurgical operations gave informed consent to be studied. None of them had neurologic or ophthalmologic disorders. Their ages ranged from 21 to 40 yr. No premedication was given to the subjects.

The 10–20 international system of electrode placement was used.[7] Chlorided silver disk electrodes were affixed to the scalp with collodion. The evoked potentials were recorded from the left or right occipital electrode (O_1 or O_2) in reference to linked ear electrodes (A_1, A_2) using the frontal electrode (F_z) as a ground. Impedance was maintained at less than 3,000 ohm. The bandpass filter was set at 1–200 Hz. The sensitivity of the recording amplifier was set at 100 μV full scale (peak to peak). An array of ten light-emitting diodes was positioned over the patient's closed eyes. Monocular flash stimulus was presented at the rate of 1.9 Hz with a duration of 10 ms. Each averaging epoch was set at 250 ms, with a total of 100 repetitions. The evoked potentials were recorded with a Nicolet Pathfinder I® (Nicolet Biomedical Instruments, Madison, WI).

As a control, evoked potentials were recorded before induction of anesthesia. Then, anesthesia was induced with 0.05 mg/kg of *d*-tubocurarine, 4–5 mg/kg of thiopental, and 1.5 mg/kg of succinylcholine iv. Anesthesia was maintained by administering various concentrations of isoflurane in 100% oxygen or in a mixture of 40% oxygen and 60% nitrous oxide. Vecuronium was given as needed to maintain muscle relaxation and controlled ventilation. End-expiratory isoflurane concentration was measured with an Engstrom Emma® gas analyzer equipped with a Flextube® Humidifier. End-tidal CO_2 was monitored with a Datex® CO_2 Monitor, and maintained at 33–40 mmHg by mechanical ventilation. Body temperature was sustained between 35–37° C, while systolic arterial blood pressure was maintained within ±25% of the preoperative level with isoflurane and an iv infusion of lactated Ringer's solution. The VEPs were recorded at 0.6, 0.9, 1.2, 1.5, and 1.8% of the isoflurane in 100% oxygen. The VEPs were also recorded in randomly selected subjects at 0.6, 1.2, and 1.8% of the isoflurane level in a 40% oxygen–60% nitrous oxide mixture. Each anesthetic end-tidal concentration was maintained for 15 min prior to recording. At least two individual VEPs were recorded at each anesthetic concentration. The order of the concentrations was randomized.

For data analysis, a one-way analysis of variance and Student-Newman-Keuls multiple comparison test were used to compare different anesthetic states. Paired Student's *t* test was used to evaluate the effects of nitrous oxide. A *P* value below 0.05 was considered statistically significant.

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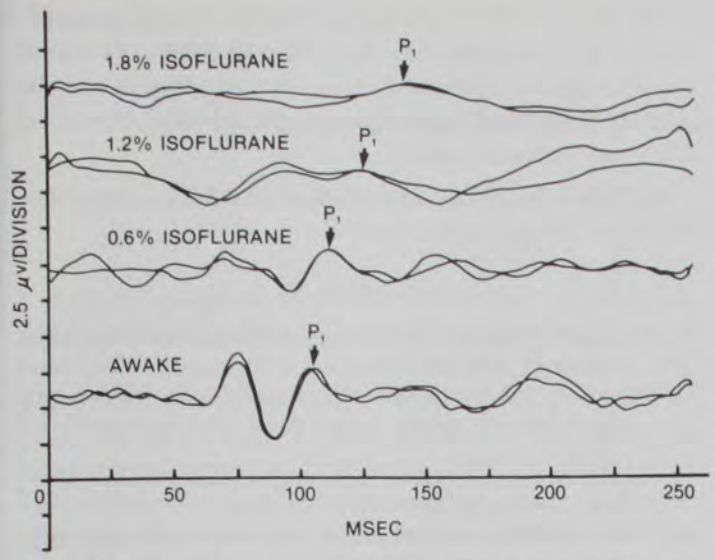

FIG. 1. Visual evoked potential (VEP) recording obtained from one patient at different end-expiratory isoflurane concentrations in 100% oxygen. Two separate tracings obtained during each condition have been superimposed.

RESULTS

The VEPs were obtained in a reproducible manner in all subjects. However, with concentrations of isoflurane above 1.8%, the P1 could not be assessed due to the decrease of the amplitude. Typical VEP waveforms from one patient are shown in figure 1. Duplications of the waveforms are superimposed.

Latencies of the P1 increased with increasing concentrations of isoflurane (table 1). The analysis of variance showed that the effect of anesthetic depth on the latency of the P1 was significant at a level of $P < 0.001$. Multiple comparison procedures showed that the prolongation of the latency was statistically significant at or above 0.9% compared with the awake state. It was not statistically significant at 0.6%. Differences of latencies between two consecutive levels of isoflurane were statistically insignificant except for the one between 0.6% and 0.9%. Adding 60% nitrous oxide to 0.6% and 1.8% isoflurane significantly increased the latency of the P1. However, adding 60% nitrous oxide to 1.2% isoflurane did not significantly increase the latency (table 2).

The amplitude of the P1 markedly decreased from 5.94 ± 2.37 μV in the awake state to 3.36 ± 2.21 μV at 0.6% isoflurane concentration, as shown in table 3. The effect of adding 60% nitrous oxide on the amplitude was not significant, as shown in table 4.

DISCUSSION

Many factors other than anesthetic agents can affect the recording of evoked potentials. Hypothermia will increase latency.[8,9] We controlled the temperature within a reasonably narrow range. Because CO_2 tension may also affect the sensory evoked potentials,[10] we minimized its fluctuation by controlled ventilation. Premedication was eliminated in order to avoid possible effects on the VEP.[4] To minimize the effects of thiopental, the evoked potentials were recorded at least 20 min after induction. Arterial

TABLE 1. Mean Latencies (ms ± SD) of P1 of VEP with Isoflurane Alone

End-tidal Isoflurane Concentration	Latency (ms ± SD)	Significance Compared with Control	Significance Compared with Previous Concentration
0% (awake) (n = 12)	102.6 ± 8.9		
0.6% (n = 11)	107.6 ± 10.7	NS	NS
0.9% (n = 12)	116.4 ± 8.1	$P < 0.005$	$P < 0.05$
1.2% (n = 12)	122.2 ± 8.7	$P < 0.001$	NS
1.5% (n = 11)	129.9 ± 8.8	$P < 0.001$	NS
1.8% (n = 12)	132.7 ± 15.0	$P < 0.001$	NS

VEP = visual evoked potential, NS = no statistical difference.

TABLE 2. Mean Latencies (ms ± SD) of P1 of VEP with Isoflurane plus 60% Nitrous Oxide

End-tidal Isoflurane Concentration	Isoflurane Alone	Isoflurane plus 60% Nitrous Oxide	Significance of Difference
0.6% (n = 8)	107.7 ± 11.0	114.4 ± 6.8	$P < 0.025$
1.2% (n = 8)	122.9 ± 3.6	127.3 ± 6.3	$P < 0.1$*
1.8% (n = 8)	131.4 ± 10.5	136.8 ± 12.5	$P < 0.05$

* No statistical difference.

TABLE 3. Mean Amplitudes (μV ± SD) of P1 of VEP with Isoflurane Alone

End-tidal Isoflurane Concentration	Amplitudes (μV ± SD)	Significance Compared with Control	Significance Compared with Previous Concentration
0% (n = 12)	5.94 ± 2.37		
0.6% (n = 11)	3.36 ± 2.21	$P < 0.001$	$P < 0.001$
1.2% (n = 12)	2.06 ± 1.38	$P < 0.001$	NS
1.8% (n = 12)	1.23 ± 0.79	$P < 0.001$	NS

NS = no statistical difference.

TABLE 4. Mean Amplitudes (μV ± SD) of P1 of VEP with Isoflurane plus 60% Nitrous Oxide

End-tidal Isoflurane Concentration	Isoflurane Alone	Isoflurane plus 60% Nitrous Oxide	Significance of Difference
0.6% (n = 8)	3.78 ± 2.44	3.29 ± 1.88	NS
1.2% (n = 8)	1.57 ± 0.51	1.85 ± 1.70	NS
1.8% (n = 8)	1.07 ± 0.79	1.65 ± 1.48	NS

NS = no statistical difference.

blood pressure was maintained at the preanesthetic level as much as possible. To maintain a low anesthetic level such as 0.6% isoflurane in 100% oxygen, the evoked potentials were recorded when there was minimal or no surgical stimulus.

Our study shows that the latency of the P1 of the VEP was prolonged at or above 0.9% of isoflurane. This finding is similar to that of Uhl *et al.*, who also found that the latency of the VEP was prolonged with an increased concentration of halothane.[5] Neither our study nor theirs showed any significant differences among the different concentrations of anesthetics; therefore, VEP would not be a useful method of monitoring the depth of anesthesia.

Manninen *et al.* found that isoflurane significantly increased the latency of peaks III, IV, and V of brain stem auditory evoked potentials (BAEP) at all end-tidal concentrations that were studied.[11] In our study of the VEP, isoflurane increased the latency of the P1 much more than it did in the BAEP in their study. Our study, as well as that of Manninen *et al.*, found no consistent influence of nitrous oxide on evoked potentials. Manninen *et al.* found no consistent change in the amplitude of the BAEP. To the contrary, our study on the VEP showed that isoflurane anesthesia significantly decreased the amplitude of the P1. These results reflect the finding that cortical evoked potentials are, in general, more sensitive to the effects of anesthetic agents than are the subcortical ones.

As expected, our finding is similar to that of Peterson *et al.*, who found that isoflurane significantly decreased the amplitude and increased the latency of the peaks in cortical somatosensory evoked potentials.[12] Burchiel *et al.* found that enflurane increased the amplitude of the VEP by three- to fivefold at 2.5–3.7%, while our study on isoflurane showed a marked decrease in the amplitude of the VEP at a high concentration.[6] Isoflurane, unlike enflurane, does not produce seizure activity in an electroencephalogram at a high concentration. Rather, it decreases the amplitude and frequency of the electroencephalogram.[13–15]

These various effects of different anesthetic agents on the VEP will help in the understanding of the function of anesthetic agents on the central nervous system. During neurosurgical procedures involving the visual pathways, interpretation of the VEP should be performed, recognizing the possible influence of anesthetics such as isoflurane. Russ *et al.* showed that neuroleptanalgesia with fentanyl, droperidol, and nitrous oxide increased the latency of the P2 by 10%, with no significant changes in amplitude.[16] To minimize the effects of isoflurane, its concentration may be decreased and other anesthetics may be added. Anesthetic agents that have minimal effects on VEP may be used instead.

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References

1. Chiappa KH, Ropper AH: Evoked potentials in clinical medicine. I. N Eng J Med 306:1140–1150, 1982
2. Feinsod M, Selhorst JB, Hoyt WF, Wilson CB: Monitoring optic nerve function during craniotomy. J Neurosurg 44:29–31, 1976
3. Grundy BL: Intraoperative monitoring of sensory evoked potentials. ANESTHESIOLOGY 58:72–87, 1983
4. Domino EF: Effects of preanesthetic and anesthetic drugs on visual evoked responses. ANESTHESIOLOGY 28:184–191, 1967
5. Uhl RR, Squires KC, Bruce DL, Starr A: Effects of halothane anesthesia on the human cortical visual evoked response. ANESTHESIOLOGY 53:273–276, 1980
6. Burchiel KS, Stockard JJ, Myers RR, Bickford RG: Visual and auditory responses during enflurane anesthesia in man and cats. Electroencephalogr Clin Neurophysiol 39:434, 1975
7. Jasper HH: The ten–twenty electrodes system. Electroencephalogr Clin Neurophysiol 10:371–375, 1958
8. Reilly EL, Kondo C, Brunberg JA, Doty DB: Visual evoked potentials during hypothermia and prolonged circulatory arrest. Electroencephalogr Clin Neurophysiol 45:100–106, 1978
9. Russ W, Kling D, Loesevitz A, Hempelmann G: Effect of hypothermia on visual evoked potentials in humans. ANESTHESIOLOGY 61:207–209, 1984
10. Nakagawa Y, Ohtsuka K, Tsuru M, Nakamura N: Effects of mild hypercapnia on somatosensory evoked potentials in experimental cerebral ischemia. Stroke 25:275–278, 1984
11. Manninen PH, Lam AM, Nicholas JF: The effects of isoflurane and isoflurane–nitrous oxide anesthesia on brainstem auditory evoked potentials in humans. Anesth Anal 64:43–47, 1985
12. Peterson DO, Drummond JC, Todd MM: Effects of halothane and isoflurane on somatosensory evoked potentials in man (abstract). ANESTHESIOLOGY 61:A344, 1984
13. Weigh JL, Garman JK, Harp JR: The electroencephalographic pattern during anesthesia with Ethrane®: Effects of depth of anesthesia, $PaCO_2$ and nitrous oxide. ANESTHESIOLOGY 35: 482–487, 1971
14. Eger EI II, Stevens WC, Cromwell TH: The electroencephalogram in man anesthetized with Forane®. ANESTHESIOLOGY 35:504–508, 1971
15. Homi J, Konchigeri HN, Eckenhoff JE: A new anesthetic agent Forane®: Preliminary observations in man. Anesth Analg 51: 439–477, 1972
16. Russ W, Luben V, Hempelmann G: Der Einfluss der Neuroleptanalgesie auf das visuelle evozierte Potential (VEP) des Menschen. Anaesthesist 31:575–578, 1982