

## Effects of Fentanyl Anesthesia on Visual Evoked Potentials in Humans

OAK ZA CHI, M.D.,\* CARRIE L. MCCOY, M.D.,† CRISTINE FIELD, R.E.E.G.T.‡

Monitoring the function of the central nervous system during anesthesia and surgery may permit altered neurologic function to be detected early so that appropriate intervention can occur. Recording visual evoked potentials (VEP) is one way to detect injury during procedures involving the visual pathway, such as transphenoidal or anterior fossa surgery.<sup>1-3</sup> The VEP is elicited by flashes coming from light-emitting diodes mounted on goggles placed over the patient's closed eyes. The VEP has a prominent peak at about 100 msec after stimuli. This peak, which is called the P100, is thought to arise in the striated and parastriated visual cortex.<sup>3,4</sup> Changes in the latency and amplitudes of this P100 peak are affected by several factors, including anesthetic agents and surgical stimuli. Since the effects of the anesthetic agents on the VEP can present similar pictures to those of the surgical injury, it is necessary to define how the anesthetic agents themselves affect the VEP. Uhl *et al.* demonstrated that the latency of the P1(P100) of the VEP was prolonged by halothane.<sup>5</sup> Burchiel *et al.* showed that the amplitude of the VEP was increased at high concentrations of enflurane (2.5-3.7%).<sup>6</sup> A recent study showed that isoflurane increased the latency and decreased the amplitude of the P1(P100) in the VEP.<sup>7</sup> Fentanyl-nitrous oxide anesthesia slightly increased the latency of the VEP with no significant change in the amplitude.<sup>8,9</sup> Because fentanyl in high doses is increasingly used alone to produce anesthesia in patients with cardiac dysfunction, and because such patients may require neurosurgical procedures involving the visual pathway, the purpose of this study was to determine the effects of the high doses of fentanyl on the VEP in humans.

## MATERIALS AND METHODS

This study was approved by our Institutional Review Board. Twelve consenting patients undergoing coronary artery bypass grafting were studied. Their mean age was 53.9 yr ( $\pm 7.9$  SD), while their mean weight was 72.4 kg ( $\pm 10.8$  SD). None of the patients had serious neurologic or ophthalmologic disorders. Recording techniques are described in table 1.<sup>10</sup> The day before surgery, the VEP was recorded as a control. On the day of their surgery, each patient received an intramuscular injection of 0.1 mg/kg of morphine and 0.4 mg of scopolamine as premedication. Their regular preoperative cardiac medications were continued up to the time of the operation. In the operating room, prior to induction of anesthesia, a peripheral venous catheter, a radial artery catheter, and a Swan-Ganz catheter were inserted, while the electrocardiogram and blood pressure were monitored. A warming blanket was placed under the patient beforehand. Cardiac output and arterial blood gases were measured. A Nellcor® Pulse Oximeter sensor was applied on the patient's index finger and a Stat-Temp® temperature sensor was applied to the patient's forehead. A pair of opaque goggles equipped with arrays of light-emitting diodes, as described in table 1, was placed over the patient's closed eyes, after which VEP were recorded to assess the effects of premedication. After this recording (pre-induction VEP), anesthesia was induced with incremental doses of fentanyl 10  $\mu$ g/kg. Each incremental dose was given over a period of 1 min. Pancuronium 0.1 mg/kg was given during induction. Each patient was ventilated with a mask and 100% oxygen. End-tidal CO<sub>2</sub> was measured with a Datex® CO<sub>2</sub> Monitor. Systolic blood pressure was maintained within  $\pm 15\%$  of the preoperative level with infusion of nitroglycerin, phenylephrine, and crystalloid. The VEP was recorded after each incremental dose of fentanyl. Each VEP recording took 1-2 min. After a total induction dose of fentanyl, which varied from 60-90  $\mu$ g/kg, lidocaine (100 mg iv) was administered and the trachea intubated. Ten minutes after intubation, the VEP was again recorded (post-induction). During this 10-min period, there was no surgical stimulus, and no additional fentanyl was given. From the VEP recordings, the first complex of a prominent negative and a prominent positive peak were identified. These peaks were designated N70 and P100, respec-

\* Assistant Professor, Anesthesiology.

† Instructor, Anesthesiology.

‡ Electrophysiology Technologist.

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Address reprint requests to Dr. Chi: Department of Anesthesia, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, One Robert Wood Johnson Place, CN-19, New Brunswick, New Jersey 08903.

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TABLE 1. Parameters Used in Recording the VEP

Stimulation:	Mode	Binocular flash stimulation
	Source	LED arrays on opaque binocular goggles placed over closed eyes
Recording:	Duration	10 msec
	Rate	1.9 Hz
	Electrodes	Chlorided silver disc electrodes affixed with collodion
	Montage*	Oz-Cz
	Ground	Mastoid
	Filters	1-100 Hz
	Sensitivity	100 $\mu$ v full scale
	Sweep	500 msec
Time		
Impedance	<3000 ohm	
Repetition	100	

Nicolet Pathfinder I (Nicolet Biomedical Instruments, Madison, WI) was used in this study.

\* The 10-20 international system of electrode placement was used.<sup>10</sup>

tively. Latencies of N70 and P100 were defined. Amplitude was measured as the vertical difference between the N70 and the P100.<sup>11</sup> Control, pre-induction, and

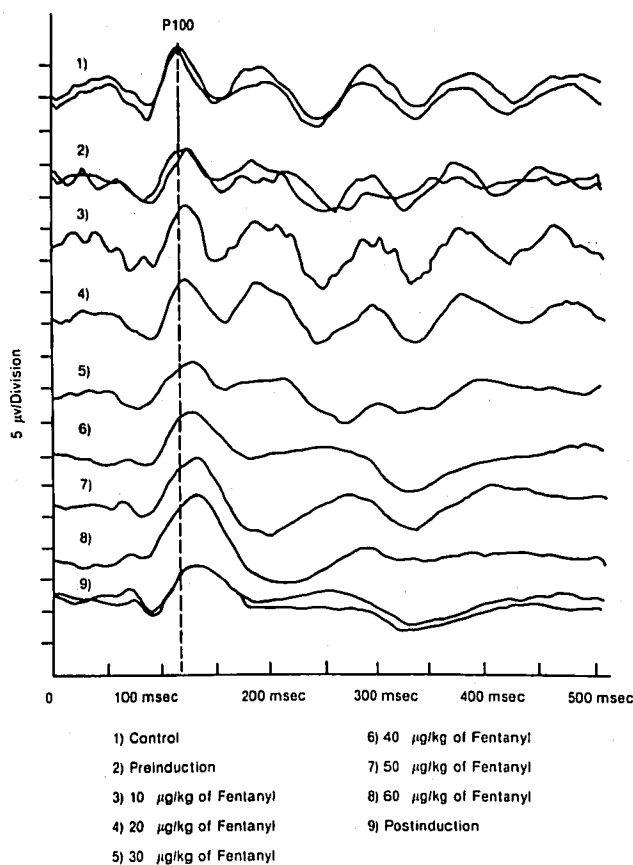


FIG. 1. The VEP recording from a patient at various time points during the study. This patient had a total of 60  $\mu$ g/kg of fentanyl during induction.

post-induction recordings were made in duplicate to ascertain reproducibility. Time constraints did not allow duplicate recordings during induction. Data from the following time points were statistically analyzed: 1) the day before surgery (control); 2) after premedication, prior to induction (pre-induction); 3) after 10, 20, 30, 40, 50, and 60  $\mu$ g/kg of fentanyl and 10 min after the last increment of fentanyl (post-induction). Analysis of variance with repeated measures and the Student-Newman-Keuls multiple comparison test were performed. A *p* value below 0.05 was considered statistically significant.

## RESULTS

During the recording of the VEP, end-tidal CO<sub>2</sub> was maintained 33-40 mmHg. Oxygen saturation was 99-100%, while the temperature ranged from 36.1-36.6° C. Systolic blood pressure was maintained within  $\pm$ 15% of the preoperative level. The time interval between premedication and the recording of the pre-induction VEP varied between 90 and 120 min. The total dose of fentanyl before tracheal intubation was 60-90  $\mu$ g/kg, while the time between the first dose of fentanyl and tracheal intubation ranged from 14-26 min. No patient experienced any discomfort or injury from the study.

Satisfactory wave forms were obtained at all recorded time points in ten of the 12 patients. Two patients from whom data could not be obtained were excluded from the statistical analysis.

There was much variation in wave amplitude among individual patients. As the dose of fentanyl increased, the wave forms tended to become simpler because of a decreasing number of small peaks, thus allowing the P100 to become easier to identify. The VEP recording from a patient is shown in figure 1.

There were no significant differences at any point in the latencies of either the N70 or the P100 (table 2). No significant change was observed among incremental doses of fentanyl. In contrast, there was a significant decrease in amplitude between control and pre-induction (-22%), and between pre-induction and each increment of fentanyl.

## DISCUSSION

The latencies of the principal peaks of the VEP are longer than those of the brainstem auditory evoked potentials and somato-sensory evoked potentials. This makes the VEP relatively unstable and vulnerable to many factors.<sup>12</sup> Temperature will affect the VEP as described by Russ *et al.* and others.<sup>13,14</sup> In our study, forehead temperature remained between 36.1-36.6° C. After tracheal intubation, the esophageal temperature

TABLE 2. Latencies and Amplitudes of the Visual Evoked Potentials (VEP) at Control, Pre-induction, after Incremental Doses of Fentanyl, and Post-induction (10 Min After Induction)

	Latency (ms)		Amplitude ( $\mu$ V) N70-P100 Mean $\pm$ SD (n = 10)
	N70 Mean $\pm$ SD (n = 10)	P100 Mean $\pm$ SD (n = 10)	
Control	81.1 $\pm$ 10.8	122.1 $\pm$ 22.2	15.39 $\pm$ 5.59
Pre-induction	79.8 $\pm$ 13.8	123.5 $\pm$ 18.4	12.01 $\pm$ 6.34*
After 10 $\mu$ g/kg	85.7 $\pm$ 13.5	122.7 $\pm$ 13.7	9.22 $\pm$ 5.14†§
After 20 $\mu$ g/kg	88.2 $\pm$ 13.9	123.3 $\pm$ 15.5	8.20 $\pm$ 4.52†§
After 30 $\mu$ g/kg	88.5 $\pm$ 10.4	122.8 $\pm$ 14.7	8.41 $\pm$ 3.89†‡
After 40 $\mu$ g/kg	87.7 $\pm$ 8.5	124.9 $\pm$ 16.7	7.71 $\pm$ 3.94†‡
After 50 $\mu$ g/kg	87.8 $\pm$ 10.1	126.8 $\pm$ 17.3	8.36 $\pm$ 4.70†§
After 60 $\mu$ g/kg	85.6 $\pm$ 11.1	125.7 $\pm$ 17.5	8.14 $\pm$ 4.61†§
Post-induction	84.0 $\pm$ 6.5	126.6 $\pm$ 19.6	9.01 $\pm$ 5.44†§
P Significance	P > 0.05 NS	P > 0.25 NS	P < 0.0005 S

S = statistically significant; NS = statistically not significant.  
\* Compared with control,  $0.005 < P < 0.01$ .  
† Compared with control,  $P < 0.001$ .  
‡ Compared with pre-induction,  $0.01 < P < 0.025$ .  
§ Compared with pre-induction,  $0.025 < P < 0.05$ .

was monitored and compared with the temperature of the forehead which confirmed the narrow range of temperature change during the study period. Arterial CO<sub>2</sub> tension may also affect sensory evoked potentials.<sup>6,15</sup> In our study, end-tidal CO<sub>2</sub> was kept within a reasonably narrow range of 33–40 mmHg. Hypoxia can affect the VEP,<sup>16,17</sup> and oxygen saturation was maintained at 99–100%. Smith found that changes in systolic blood pressure down to 80 mmHg did not affect the VEP.<sup>18</sup> When systolic blood pressure fell below 80 mmHg, he found that there was a progressive decrease in the amplitude. In our study, systolic blood pressure was maintained within  $\pm 15\%$  of the preoperative levels, and none of the patients had blood pressure below 80 mmHg during the study period.

Our study showed that there was a 22% decrease in the amplitude of the VEP after premedication with morphine and scopolamine. Only anecdotal and insufficient studies are available on the effects of the individual premedicant on the VEP.<sup>19,20</sup> It is difficult to say which agent caused the observed changes after premedication in our study.

The effects of the size of the pupil and the amount of the light hitting the retina on the VEP should be considered. Kriss *et al.* described a significant increase in the latency of the flash VEP through the closed eyelids when compared with the open eyes.<sup>21</sup> Others have

found that the VEP amplitude was increased with the pupillary dilatation.<sup>20,22</sup> In our study, all the VEP recordings, including controls, were done through closed eyelids. However, the observed decreases in amplitudes of the VEP after incremental doses of fentanyl in our study could have been caused by pupillary constriction induced by fentanyl.

Sebel *et al.* noticed that, with an increased concentration of nitrous oxide, the latency of the VEP increased significantly, whereas the amplitude was decreased.<sup>23</sup> In our study, fentanyl did not affect latencies, but decreased the amplitude. However, in other studies, fentanyl-nitrous oxide anesthesia increased latencies with no significant changes in the amplitude.<sup>8,9</sup> Apparently, the effects of fentanyl and nitrous oxide on the VEP are not simply additive. This feature of anesthetic effects on the VEP needs further exploration.

In conclusion, the VEP is resistant to the effects of a high dose of fentanyl. Interpretation of the VEP during fentanyl anesthesia can be performed without difficulty.

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## Falsely Normal Saturation Reading with the Pulse Oximeter

ANDREW T. COSTARINO, M.D.,\* DEBORAH A. DAVIS, M.D.,† THOMAS P. KEON, M.D.‡

Several studies have documented excellent correlation between pulse oximetry and simultaneous direct arterial samples for determining oxygen saturation.<sup>1-3</sup> This reliable non-invasive monitor has been known to be helpful in rapid detection of intraoperative and postoperative hypoxemia.<sup>4-6</sup> Despite its value, there are several well-known limitations to pulse oximetry.<sup>7</sup> We wish to report a case in which a pulse oximeter reading of 100% persisted in spite of clinical cyanosis and extubation of the trachea.

### REPORT OF A CASE

The patient was a 6-day-old, 2.6-kg boy with choanal atresia brought to the operating room for direct examination and surgical treatment of this disorder. He was the product of a full-term, uncomplicated pregnancy and delivery, to a 35-yr-old, gravida 3, para 1 mother. The Apgar scores were 8 (at 1 min) and 9 (at 5 min). At 6 h of age, the infant was noted to have respiratory distress, and the diagnosis of

choanal atresia was made when feeding catheters could not be passed through either nares. Other causes of neonatal respiratory distress were ruled out. A patent airway was maintained with the use of a McGovern nipple (a plastic nipple with a large hole cut in it).

On arrival in the operating room, the patient appeared comfortable in room air, with mild respiratory retractions. Arterial blood gases and oxygen saturation determined during the preoperative evaluation were normal. The rest of his physical examination was unremarkable, as were complete blood count, urinalysis, serum bilirubin, and a chest radiograph.

Induction of anesthesia was accomplished by allowing the child to spontaneously inhale halothane and nitrous oxide in oxygen. Pancuronium 0.3 mg was given iv, and a 3.0 mm I.D. oral RAE performed tracheal tube was inserted into the trachea. Following taping on the tracheal tube to the skin over the mandible, breath sounds were noted to be equal to auscultation bilaterally.

Monitors included a precordial stethoscope, electrocardiogram, automatic blood pressure cuff, temperature probe, and a pulse oximeter.§

The infant was positioned for surgery on a shoulder role with the head in extension and, shortly after, was noted to be cyanotic. Although the pulse oximeter§ indicated a pulse of 180 and a saturation of 100%, persistent cyanosis of the lips, tongue, and skin, and the decreased compliance of the bag with hand ventilation, suggested displacement of the tracheal tube. Accidental extubation of the trachea was confirmed by direct laryngoscopy, and the patient was reintubated without difficulty. Surgery proceeded without further incident. The immediate postoperative course, and a re-examination at 24 h, did not suggest any problems associated with the brief period of cyanosis.

During the surgery, it was recognized that, when the surgical light illuminated the pulse oximeter sensor (Nellcor D-20 digit oxisensor), the display on the pulse oximeter would indicate 100% saturation and

\* Assistant Professor of Anesthesia and Pediatric Critical Care, The Children's Hospital of Philadelphia.

† Assistant Professor of Anesthesia and Pediatrics, St. Christopher Hospital for Children.

‡ Associate Professor of Anesthesia, The Children's Hospital of Philadelphia.

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Address reprint requests to Dr. Keon: Department of Anesthesia and Critical Care, 34th Street and Civic Center Boulevard, Philadelphia, Pennsylvania 19104-4399.

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§ Nellcor Pulse Oximeter Model N-100c, Hayward, California (945454), with Nellcor D-20 digit oxisensor.

¶ Narco-Pilling Source, Narco Scientific, Fort Washington, Pennsylvania 19034.