Olfactory evoked potentials: experimental and clinical studies

MASANORI SATO, M.D., NAMIO KODAMA, M.D., TATSUYA SASAKI, M.D., AND MAMORU OHTA, M.D.

Department of Neurosurgery, Fukushima Medical School, Fukushima, Japan

Recently in neurosurgery, various sensory evoked potentials have been used for evaluating neurological function as a means for objective assessment or intraoperative monitoring. However, objective methods for evaluating olfactory functions, which are also important for daily living, have not yet been developed.

Following surgery near the anterior fossa, some patients experience loss of olfactory functions. Eriksen and colleagues reported a high incidence of ipsilateral anosmia (89%) in patients who underwent aneurysm surgery that required a frontotemporal approach. Suzuki, et al., reported that it was necessary and possible to preserve the olfactory tracts during bifrontal craniotomy. However, even when the olfactory system has been preserved morphologically, olfaction often is impaired. In such cases, the intraoperative monitoring of olfactory evoked potentials (OEPs) is useful for functional preservation. Because the complaints of patients whose olfactory functions have been injured are often severe, efforts should be made to preserve olfactory functions during surgical manipulations.

Objective methods for evaluating olfactory functions have not yet been established. Animal experiments and clinical studies focused on the recording of OEPs using chemical stimulation have been reported. However, in intraoperative monitoring, it is impossible to keep the conditions of chemical stimulation constant because the washout time of chemical substances adhering to the olfactory mucosa is prolonged. Potentials that are evoked following repetitive chemical stimulation consequently are not reliable.

On the other hand, electrical stimulation allows quantification of stimulus intensity and repetitive stimulation under constant conditions with relative ease. In earlier animal studies, potentials from the olfactory system that had been evoked by electrical stimulation were examined to study olfactory pathway physiology. However, recordings from the olfactory tract following electrical stimulation of the olfactory mucosa have not previously been reported. In the present study, we recorded OEPs in dogs and humans to develop an objective method for evaluating olfactory functions.

Experimental Study

Experiments were performed using 25 adult mongrel dogs, each weighing 10 to 15 kg. Anesthesia was induced with an intravenous injection of 25 mg/kg sodium pentobarbital and maintained by additional administration at 2.5 mg/kg/hour to ensure that the animals would be free from pain. After tracheal intubation, PaO2 and PaCO2 were adjusted and maintained at 90 to 120 mm Hg and 35 to 45 mm Hg, respectively. A catheter was inserted into the femoral artery for the measurement of blood pressure and the collection of blood.
Olfactory evoked potentials

Fig. 1. Photograph showing a soft fiber catheter, 0.7 mm in diameter, and the stimulating electrode attached to the external tube.

Fig. 2. Visualization of the olfactory mucosa through a soft fiber catheter displaying the olfactory mucosa (OM), the nasal septum (NS), and the superior nasal concha (SNC).

Ringers’ lactate solution, used as a maintenance fluid, was infused through a peripheral vein at the rate of 5 to 10 ml/kg/hour. Body temperature (rectal) was maintained with a heating blanket at 37˚C to 38˚C.

Each dog was placed prone. The nasal bone was removed, and the olfactory mucosa was exposed and identified by its slightly yellow color. Two silver ball electrodes were affixed, approximately 2 mm apart, to the olfactory mucosa to be used for electrical stimulation. These electrodes were connected to the isolator of an electrical stimulator. The mucosa was stimulated with a 10- to 50-V rectangular pulse, 0.1 to 0.2 msec in duration, at a frequency of 0.1 to 10 Hz. Alternating current stimulation was used on occasion to reduce the current spread.

A silver ball electrode was affixed to the olfactory tract and connected to the cathode of an amplifier. Another silver ball electrode was attached to the parietal lobe, which was believed to be free from olfactory projections and electrically stable. Potentials from the olfactory tract were passed through a 1- to 1500-Hz bandpass filter. The response evoked by electrical stimulation of the olfactory mucosa was processed and recorded each time or by averaging 50 signals. Upturned waves on the recording were defined as negative potentials. In addition, a stainless-steel needle electrode for recording was inserted into the scalp of the temporal region near the olfactory tract and attached. Following stimulation of the olfactory tract, the response at the scalp was recorded and compared to the response obtained from the olfactory tract.

The OEPs were analyzed for the following: 1) influence of artifacts in electrical stimulation; 2) influence of the electromyogram; 3) influence of the trigeminal nerve; 4) specificity of the site of stimulation; 5) changes following sectioning of the olfactory nerve; and 6) influence of the frequency of electrical stimulation. With the frequency set at 1 Hz or 5 Hz, evoked potentials were recorded from the beginning of stimulation until the 100th stimulation.

Clinical Study

Recording of OEPs was performed after electrical stimulation of the olfactory mucosa in 10 patients (aged 33–65 years; six cases of brain tumor, four cases of aneurysm) who had undergone bifrontal or frontotemporal craniotomy. All of these patients were at risk of olfactory impairment from anterior fossa surgery and required an objective evaluation of olfactory function. The consent for the test was obtained from the patients or their families prior to the examination. After anesthesia was induced in the patient, the nasal cavity was visualized through a soft fiber catheter, 0.7 mm in diameter (Fig. 1). Before testing, 10 μg/ml epinephrin (1 mg of 0.1% epinephrin dissolved in 100 ml saline) was administered and vasoconstriction was induced. A dipolar silver ball electrode was attached to the tip of the external tube around the soft catheter. It enabled us to obtain a direct view and to approach the yellowish olfactory mucosa at the olfactory fissure between the nasal septum and the superior nasal concha (Fig. 2). Thus the dipolar silver ball electrode could be affixed to the olfactory mucosa. This electrode was connected to an isolator of an electrical stimulator, and the mucosa was stimulated with a 1- to 7-mA rectangular pulse, 0.1 msec in duration at a frequency of 0.1 to 5 Hz.

Following craniotomy, a silver ball electrode that served as a recording electrode was placed on the exposed olfactory tract and another silver ball electrode that served as a silent electrode was placed on the frontal lobe. Fifty signals were averaged and processed for recording. In addition, a stainless-steel needle electrode for recording was inserted and affixed to the scalp in the frontotemporal region (F7; International 10–20 system) and a silent electrode was placed in the vertex. The OEPs in humans were analyzed according to the same criteria used in the animal studies.

Sources of Supplies and Equipment

The silver ball electrodes (model 45182) and stainless-steel needle electrodes (model 45244) used in the studies were obtained from NEC Medical Systems, Corp., Tokyo, Japan. The electrodes were connected to the isolator (model SS-101J) of an electrical stimulator (model SEN-1101), both of which were manufactured by Nihon Kohden Corp., Tokyo, Japan. An NEC signal processor (model 77T07A) and an NEC X-Y recorder (model 8U16) were used in assessing the evoked response.

In the clinical study, the soft fiber catheter (model AS-001) used to visualize the nasal cavity was obtained from Fukuda Electronics Corp., Tokyo, Japan.

Results

Experimental Study

Stable recordings of OEPs were obtained using electrical stimulation of the olfactory mucosa at 20 V and higher (Fig. 3A). The amplitude of the evoked potential was maximum at a 50-V stimulation. The most conspicuous response from the olfactory tract was the negative peak, which had a peak latency of approximately 40 msec (mean ± standard deviation 41.04 ± 4.34 msec, 25 dogs). This peak is designated N40 wave in the following discussion. The amplitude of N40 was approximately 200 μV (201 ± 56 μV, 25 dogs). It was highly reproducible and could be readily observed with a single stimulus; however, averaging provided a smoother and more stable

J. Neurosurg. / Volume 85 / December, 1996
wave form. In addition, a positive–negative peak occasionally followed N40 wave. This peak was not as stable as N40 and its peak latency was widely scattered (56–100 msec).

Further study of the evoked potentials, including N40, yielded the following results: 1) There was no significant difference in the polarity, peak latency, or basic wave form following polarity reversal of each stimulation (Fig. 3B). 2) No significant differences in wave forms, peak latency, or amplitude were demonstrated after administration of pancuronium bromide. 3) Following trigeminal nerve transection, the N40 wave was unchanged, suggesting that it did not originate from the intracranial trigeminal nerve (Fig. 3C). 4) Electrical stimulation of the nasal mucosa did not produce distinct evoked potentials from the olfactory tract. However, evoked potentials were recorded from the trigeminal nerve, demonstrating stimulus specificity.12,21 5) After the olfactory nerve had been sectioned between the olfactory mucosa and the olfactory bulb, the evoked potential, including the N40 wave, disappeared. 6) A comparison of recordings following stimulation of the olfactory mucosa at 1 Hz or 5 Hz revealed that the amplitude of the N40 wave elicited by a stimulation at 5 Hz was reduced by approximately 60% (113 ± 29.72 µV, seven dogs) compared to that at 1 Hz (184 ± 33.04 µV, seven dogs) (Fig. 3D). At a frequency of 10 Hz, the amplitude was further reduced by approximately 30%.

Furthermore, negative potentials with a 40-msec peak latency (39.60 ± 1.49 msec, 10 dogs) were recorded from the scalp of the temporal region near the olfactory tract with a high reproducibility and were similar to tracings from the olfactory tract (Fig. 4). At a frequency of 10 Hz, the amplitude was further reduced by approximately 40 msec was nearly identical to the N40 wave from the olfactory tract; the amplitude was approximately 30 µV (28.71 ± 8.63 µV, 10 dogs). The response was not affected by electrical stimulation, electromyogram, or sectioning of the trigeminal nerve. In addition, the response disappeared after olfactory nerve sectioning.

Clinical Study

In the clinical portion of the study, the olfactory mucosa was identified by its yellowish color, which distinguished it from surrounding nasal mucosa as in the animal studies. In the 10 patients studied, the stimulating electrode was affixed to the olfactory mucosa. Electrical stimulation of the olfactory mucosa generated monophasic and occasional multiphasic potentials recorded from the olfactory tract (Fig. 5). The evoked potential was similar to the wave form observed in dogs. The peak latency of the first negative wave, designated N27, ranged from 25 to 30 msec (27.02 ± 2.12 msec, 10 dogs), and the amplitude varied between 5 and 25 µV.

Additional analysis revealed that: 1) the N27 wave was recorded with a high reproducibility and remained unaltered after administration of a muscle relaxant; 2) no potential was recorded after electrical stimulation of the nasal mucosa; and 3) as was the case in the animal study, the amplitude of the N27 wave was reduced approximately 60% by increasing the stimulation frequency from 1 Hz to 5 Hz.

In the 10 patients entered in the study, postoperative complications such as impaired sense of smell were not detected by olfactometric examination.

Discussion

We have successfully recorded OEPs from the olfactory tract in dogs and humans. In dogs, monophasic or multiphasic potentials, including the N40 wave from the olfactory tract, were obtained by electrical stimulation of the olfactory mucosa. The N40 wave arose specifically after
Olfactory evoked potentials

This potential most likely resulted from the distal spread of the OEPs from the olfactory pathway, which indicates the possibility of noninvasive recording in human subjects. The amplitude of the evoked potentials recorded from the scalp of dogs was reduced to approximately 15% of the direct olfactory tract recording. On the other hand, attempts to record from the scalp in human patients have met with failure because of the small amplitudes of the evoked potentials, which are further reduced as they pass through the skull. Because background electroencephalographic signals might mask small evoked potentials, development of a high-performance amplifier may be required to make it possible to record evoked potentials from the scalp in the future.

Although it is not currently possible to record OEPs in neurosurgical patients in a totally noninvasive manner, we believe that direct intraoperative recordings from the olfactory tract may help preserve olfactory function during neurosurgical manipulation, particularly during bifrontal or frontotemporal craniotomy. Because the procedure is simple and relatively noninvasive, it should be considered in any patient undergoing surgery near the anterior fossa.

References


J. Neurosurg. / Volume 85 / December, 1996
19. Ohno S: [Comparative studies on surface ultrastructure of olfactory epithelia.] *Otol Fukuoka* 25:677–697, 1979 (Jpn)
23. Tonoike M, Kurioka Y: [Correlation analysis of the waveforms of olfactory evoked brain potentials recorded from human scalp.] *Bull Electrotech Lab* 43:14–22, 1979 (Jpn)

Manuscript received March 4, 1996.
Accepted in final form June 10, 1996.

*Address reprint requests to:* Masanori Sato, M.D., Department of Neurosurgery, Fukushima Medical School, 1-Hikarigaoka, Fukushima 960-12, Japan.