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A comparison of the absolute amplitude of motor evoked potentials among groups of patients with various concentrations of nitrous oxide

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Abstract
Purpose. It has been shown in previous studies that nitrous oxide (N_2O) suppresses the amplitude of motor evoked potentials (MEPs) in individual subjects. In the present study, we compared the absolute amplitude and latency of MEPs among groups of patients with various concentrations of N_2O.
Methods. The subjects were 60 patients who were scheduled to undergo craniotomy with MEP monitoring. Anesthesia was induced and maintained with propofol and fentanyl. The patients were randomly assigned to one of three groups based on the concentration of N_2O: 0% N_2O (N0 group), 50% N_2O (N50 group), and 66% N_2O (N66 group). MEPs were elicited by transcranial electrical stimulation. The effect-site concentrations (ESCs) of anesthetics were calculated retrospectively. The effects of anesthetics on MEP were analyzed by analysis of covariance (ANCOVA) followed by Tukey's method.
Results. MEPs were elicited in all cases. The absolute amplitude of the MEP was significantly higher in the N0 group than in the N50 and N66 groups [4.16 ± 0.42 vs 1.00 ± 0.26 mV and 1.00 ± 0.27 mV, respectively (mean ± SD); $P < 0.05$]. In contrast, there was no significant difference in the latency of the MEP among the three groups of subjects (N0: 16.64 ± 0.72, N50: 16.78 ± 0.66, and N66: 16.82 ± 0.63 ms).
Conclusion. The results suggest that N_2O can suppress the absolute amplitude of the MEP in patients under propofol and fentanyl anesthesia. Although monitoring of MEP as a trend is feasible even if N_2O is used, the use of N_2O may be better avoided.

Key words MEP · Propofol · Fentanyl · Effect-site concentration · Nitrous oxide

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Introduction

The intraoperative motor evoked potential (MEP) is a neurological monitor used for minimizing neural injury during surgical procedures [1]. However, consideration must be given to the method used for induction and maintenance of anesthesia during surgery with monitoring of the MEP, because the MEP is easily influenced by various anesthetics [2–7]. Since some previous works demonstrated that nitrous oxide (N_2O) suppress the amplitude of MEP in individual subjects [4,5], we compared the absolute amplitude and latency of MEPs among groups of patients with various concentrations of N_2O.

Materials and methods

This study was approved and monitored by the Research Ethics Committee of Tokyo Women's Medical University, and informed consent was obtained from each patient. The subjects were 60 patients, 18 to 76 years old, who were scheduled to undergo craniotomy for brain tumor removal or aneurysm surgery. MEP monitoring was performed in patients in whom there was a possibility that surgical maneuvers would extend to the motor area or motor tract. Patients with paralysis before the operation were excluded from this study. The patients were randomly assigned to one of the three groups based on the concentration of nitrous oxide: 0% N_2O (N0 group), 50% N_2O (N50 group), and 66% N_2O (N66 group).

Before the induction of anesthesia, 2 to 3 $\mu g \cdot kg^{-1}$ of fentanyl was administered. Several minutes later, administration of propofol at a target concentration of 3 to 5 $\mu g \cdot ml^{-1}$ was initiated using a target-controlled infusion (TCI) system, Diprifusor (AstraZeneca Pharmaceuticals, Cheshire, UK) [8]. After loss of consciousness, 0.1 to 0.15 $mg \cdot kg^{-1}$ of vecuronium bromide was admin-

Table 1. Demographic characteristics of patients participating in the study[a]

Characteristic	N0 group	N50 group	N66 group
No. of patients	20	20	20
Sex (male/female)	9/11	7/13	8/12
Age (yr)	51 ± 19	50 ± 17	53 ± 15
Height (cm)	164 ± 8	160 ± 11	161 ± 10
Weight (kg)	60 ± 13	62 ± 9	59 ± 10
ASA class (I/II)	8/12	7/13	8/12
Type of surgery (BTR/AS)	16/4	15/5	16/4

[a] Values are mean ± SD. BTR, brain tumor resection; AS, aneurysm surgery

istered, and the trachea was intubated. Additional vecuronium was not administered. Anesthesia was maintained with continuous infusion of propofol by the TCI system and repeated injection of fentanyl. Before head-pinning and the start of surgery, 1 to 3 $\mu g \cdot kg^{-1}$ of fentanyl was administered, and then 0.5 to 2 $\mu g \cdot kg^{-1}$ of fentanyl was administered as needed to maintain the heart rate close to 60 to 80 bpm before and during surgery. The target concentration of propofol was adjusted in the range of 2.8 to 5.0 $\mu g \cdot ml^{-1}$ according to hemodynamics.

MEPs were elicited by transcranial electrical stimulation (train-of-five; stimulation rate, 500 Hz; square wave pulse with a time constant of 50 μs; stimulation intensity, 600 V) using a stimulator (Digitimer D185, Digitimer, Welwyn Garden City, UK). Coke Screw electrodes (A Gram, A Gram Export-Import, Glen Rock, NJ, USA) were inserted into the scalp around C3 and C4 (international ten-twenty electrode system). The anode was placed on the affected side and the cathode was placed on the unaffected side. MEPs were recorded using Neurosign 800 (Magstim, Whitland, UK) via stainless needle electrodes (1543-00, Magstim) inserted in the extremities (bilateral thenar muscles and anterior tibial muscles). Filter settings ranged between 10 Hz and 5 kHz.

The effect-site concentrations (ESCs) of the anesthetics were calculated on the basis of data in anesthetic records and the results of pharmacokinetic simulation. A three-compartment model was used for pharmacokinetic analysis, with the parameter of Marsh for propofol [9] and the parameter of Shafer for fentanyl [10]. Both blood concentration and ESC was calculated every minute using Euler's method. MEPs were elicited in the extremities and recorded throughout surgery. Data on the amplitude and latency of the MEP in the contralateral superior limb were used for analysis during periods when there were no effects of surgical maneuvers and muscle relaxant. The former is the period before starting intracranial maneuver, i.e., before incision of the dura. No effect of the muscle relaxant was confirmed by recovery train-of-four response.

The Kruskal-Wallis test followed by a post-hoc analysis using Mann-Whitney's U test with Bonferroni's correction and one-way analysis of variance (ANOVA) followed by Tukey's method were used for statistical comparison of backgrounds between groups. The effects of the anesthetics on MEP were analyzed by analysis of covariance (ANCOVA) followed by Tukey's method. A P value less than 0.05 was considered to indicate statistical significance.

Results

There were no intergroup differences in the patients' demographic characteristics (Table 1). The MEP was elicited in all cases. The absolute amplitude of the MEP was significantly higher in the N0 group than in the N50 and N66 groups [4.16 ± 0.42 mV vs 1.00 ± 0.26 mV and 1.00 ± 0.27 mV, respectively (mean ± SD); $P < 0.05$]. In contrast, there was no significant difference among the three groups in the latency of the MEP (N0: 16.64 ± 0.72; N50: 16.78 ± 0.66; and N66: 16.82 ± 0.63 ms) (Fig. 1). Figure 2 shows the relationship between the ESCs of intravenous anesthetics and the amplitude or latency of the MEP in each group.

Discussion

Suppression of the amplitude of the MEP by N_2O has also been found in previous studies [4,5]. Our data suggest that N_2O significantly decreased the absolute value of the amplitude of the MEP in the groups with 50% and 66% N_2O as compared with the group with 0% N_2O, and also caused a similar suppressive response in individual subjects. This result is notable, because suppression of the MEP by N_2O seems to overcome variability among patients by influencing factors such as slight differences in electrode placement, thickness of the scalp, and electric resistance. Therefore, monitoring of the trend in MEP is possible even if N_2O is used, although the use of N_2O should be avoided if possible. There were no significant differences among groups of subjects with various concentrations of N_2O in the latency of the MEP, a finding consistent with that of a previous study [5].

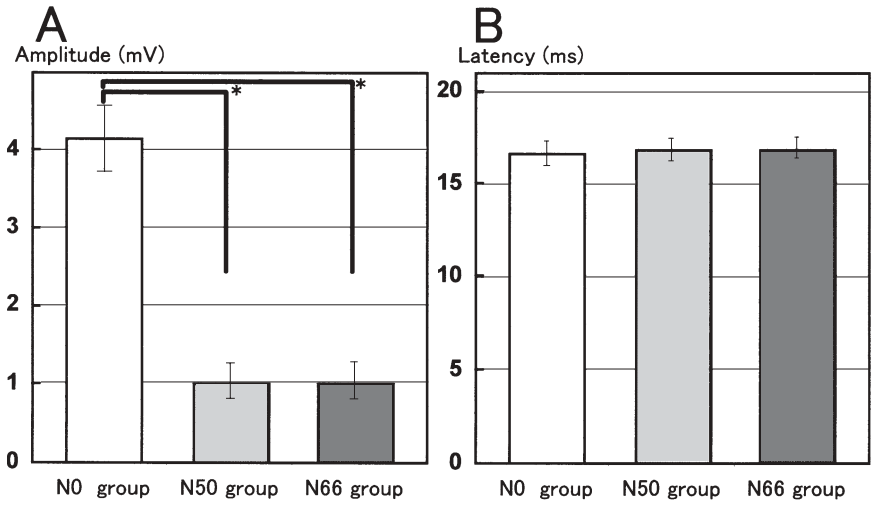

Fig. 1. Effects of nitrous oxide on the amplitude and latency of the motor evoked potential (MEP). The amplitude of the MEP was significantly higher in the N0 group than in the N50 and N66 groups (**A**). There was no significant difference among groups in the latency of the MEP (**B**). Data are expressed as mean ± SD. $*P < 0.05$ compared with that in the N0 group

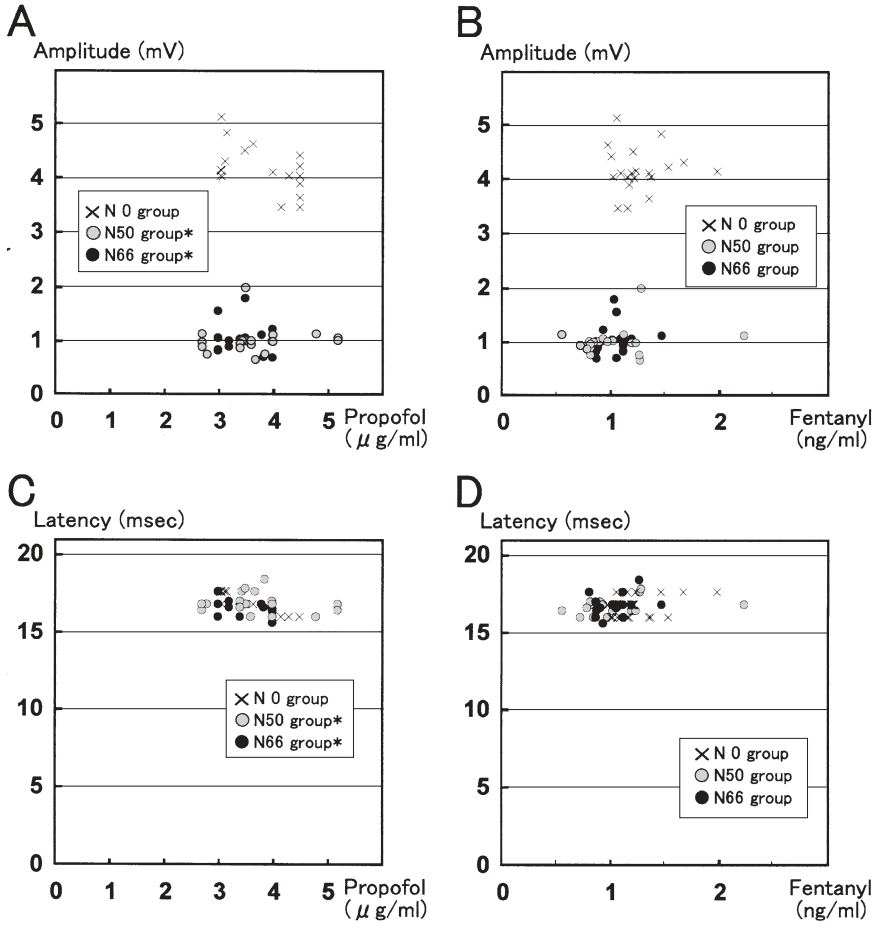

Fig. 2. Relationship between the effect-site concentration (ESC) of intravenous anesthetics and the amplitude or latency of the MEP in each group. The ESC of propofol (**A**) and that of fentanyl (**B**) had very little effect on the amplitude of the MEP. The ESC of propofol (**C**) and that of fentanyl (**D**) also had very little effect on the latency of the MEP. $*P < 0.05$ compared with the N0 group

It has been reported that an induction dose of propofol caused depression of the amplitude of the MEP [2]. Dose-dependent suppression of the amplitude of the MEP by propofol was also found in recent studies [6,7]. Although it had been thought that fentanyl at a clinical dose has no effect on the amplitude or latency of the MEP [2], recent studies have shown that the amplitude is suppressed in a dose-response fashion [6,7]. However, no such effect on the amplitude of the MEP by either of the anesthetics was seen in our study (Fig. 2). It is thought that dose-dependent depression of the MEP might have occurred in each subject. Since the

effect of the above factors on the amplitude of the MEP might have been greater than the effects of individual dose dependency at the concentrations used clinically, we believe that those effects did not appear. A limitation of our protocol is that the ESCs of propofol and fentanyl were not decided randomly, but were adjusted according to hemodynamics, which only reflected the individual requirement. Further prospective study using a protocol in which the ESCs of these anesthetics are decided randomly is needed. With respect to the latency of the MEP, no such effect on the latency of the MEP by either propofol or fentanyl was seen, a finding consistent with those of previous studies [2,6,7].

As mentioned above, the amplitude of the MEP was affected by many factors in addition to anesthetics. Therefore, it is very difficult to evaluate neurological function using the absolute value of the amplitude of the MEP, which is reduced by neurological damage. It is important, therefore, to observe the trend in amplitude in each patient.

In summary, it was found in the present study that N_2O affects the absolute value of the amplitude of the MEP among groups of patients as well as in individual patients. Although monitoring of MEP as a trend is feasible even if N_2O is used, the use of N_2O seems to be better avoided.

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