Neuroanesthesia and Intensive Care

Noxious stimuli do not modify myogenic motor evoked potentials by electrical stimulation during anesthesia with propofol-based anesthesia

[Des stimuli douloureux ne modifient pas les potentiels évoqués myogènes moteurs obtenus par stimulation électrique pendant l'anesthésie à base de propofol]

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Purpose: To investigate whether motor evoked potentials (MEP) to transcranial electrical stimulation under constant blood propofol concentration are affected by the arousing effect of surgical noxious stimuli.

Methods: Twenty patients who underwent elective spinal surgery were studied. Patients were anesthetized with 50% nitrous oxide in oxygen, fentanyl, and propofol to maintain the bispectral index (BIS) score around 50. MEP in response to a multipulse transcranial electrical stimulation at stimulus sites of C3–C4 were recorded over the right abductor pollicis brevis muscle. Changes of peak-to-peak amplitude and onset latency of MEP, BIS score before and after surgical stimuli were evaluated. Propofol plasma concentration was measured at the same time points.

Results: Both MEP amplitude and latency did not change significantly after surgical stimuli although BIS increased significantly (48 ± 6 to 58 ± 5; $P < 0.05$). Plasma propofol concentration was maintained at the same level between the two measurement points (3.3 ± 0.7 to 3.3 ± 0.7 $\mu g \cdot mL^{-1}$). There was no relation between BIS change and changes of MEP amplitude and latency, and propofol plasma concentration.

Conclusion: MEP to the transcranial electrical stimulation under a constant and clinically appropriate blood propofol concentration are not affected by surgical noxious stimuli.

Objectif : *Découvrir si les potentiels évoqués moteurs (PEM) obtenus par une stimulation électrique transcrânienne, pendant le maintien d'une concentration sanguine constante de propofol, sont influencés par l'activation des stimuli chirurgicaux douloureux.*

Méthode : *Vingt patients qui devaient subir une opération non urgente de la colonne vertébrale ont été étudiés. Ils ont reçu une anesthésie réalisée avec un mélange de protoxyde d'azote et d'oxygène à 50 %, du fentanyl et du propofol pour maintenir la valeur de l'index bispectral (BIS) autour de 50. Les PEM obtenus par une stimulation électrique transcrânienne multi-impulsionnelle aux sites de C3–C4 ont été enregistrés sur le muscle court abducteur du pouce. Les changements d'amplitude crête-à-crête et le temps de latence des PEM ainsi que le score du BIS avant et après les stimuli chirurgicaux ont été évalués. La concentration plasmatique de propofol a été mesurée aux mêmes moments.*

Résultats : *L'amplitude et la latence des PEM n'ont pas changé de façon significative après les stimuli chirurgicaux, même si le BIS a augmenté significativement (48 ± 6 à 58 ± 5; $P < 0,05$). La concentration plasmatique de propofol a été maintenue au même niveau entre les deux points de mesure (3,3 ± 0,7 à 3,3 ± 0,7 $\mu g \cdot mL^{-1}$). Il n'y avait pas de relation entre les changements du BIS et ceux de l'amplitude et de la latence des PEM, et la concentration plasmatique de propofol.*

Conclusion : *Les PEM obtenus par stimulation électrique transcrânienne, pendant le maintien d'une concentration sanguine de propofol appropriée à la situation clinique, ne sont pas influencés par les stimuli chirurgicaux douloureux.*

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THE inhibition of myogenic motor evoked potentials (MEP) observed with most anesthetic agents limits the ability to titrate anesthetic levels and achieve an adequate depth of anesthesia during intraoperative MEP monitoring.[1–10] Therefore, anesthetic concentrations are generally not modified when MEP monitoring is used. In addition, these anesthetics are usually used at relatively low doses, and patients undergoing intraoperative MEP monitoring often demonstrate symptoms of light anesthesia in response to noxious stimuli during surgery.[1–10] Ideally, anesthesia for intraoperative MEP monitoring should not inhibit MEP monitoring and, simultaneously, should provide adequate anesthesia in response to surgical stimuli.

Multiple investigators have documented the usefulness of computer processed electroencephalography (EEG), such as the bispectral index (BIS), to quantify assessment of anesthetic depth.[11–13] In general, anesthetic depth is affected by noxious stimuli. BIS appears to be sensitive to the changes in anesthetic depth produced by noxious stimuli, including surgery.[11–13] Furthermore, it is conceivable that noxious stimuli might also increase evoked potential signals, including MEP. If the arousing effect of surgical noxious stimuli affects MEP even under constant anesthetic concentration, the modification of monitoring results might lead to a misestimation of motor function. Simultaneously, adjustment of the anesthetic regimen would be required to provide adequate anesthesia against noxious stimuli. The present study was conducted to investigate whether MEP to transcranial electrical stimulation under constant blood propofol concentration are affected by the arousing effect of surgical noxious stimuli using BIS as an assessment of anesthetic depth.

Materials and methods

After Institutional approval and informed consent, 20 patients (nine men and 11 women), classified as ASA physical status I or II and scheduled to undergo elective cervical or lumbar spinal surgery, were enrolled.

All patients were premedicated with roxatidine (H_2 blocker) 75 mg orally two hours preoperatively. Anesthesia was induced with propofol 1.5–2.5 $mg \cdot kg^{-1}$, fentanyl 7–8 $\mu g \cdot kg^{-1}$ and vecuronium 0.1 $mg \cdot kg^{-1}$ and maintained with 50% nitrous oxide in oxygen, propofol 3–6 $mg \cdot kg^{-1} \cdot hr^{-1}$ and fentanyl 4–5 $\mu g \cdot kg^{-1} \cdot hr^{-1}$. After the trachea was intubated, the lungs were ventilated mechanically to maintain $PaCO_2$ between 35–40 mmHg. Systolic blood pressure was maintained at 100–130 mmHg. When hypotension or hypertension was observed, a bolus of ephedrine or nicardipine was administered.

Muscle relaxation was monitored and controlled by the following. Compound muscle action potentials from the right abductor pollicis brevis muscle (APB) in response to supramaximal electrical stimulation (constant-current square wave pulses of 0.2 msec duration) of the median nerve at the wrist were recorded as a means of assessing the degree of neuromuscular blockade. This response is known in the neurophysiologic literature as the muscle (M) response.[14] The control value was defined as that at admission to the operating room without the effect of vecuronium. The level of M-response was maintained at 40–50% of control with a continuous infusion of vecuronium. Other monitoring included the electrocardiogram, intraarterial pressure, oxygen saturation by pulse oxymetry, end-tidal CO_2 concentration, and rectal temperature.

Transcranial stimulation was performed using a multipulse device (D-185; Digitimer, Welwyn, Garden City, UK). A train-of-five pulses with an interstimulus interval of 2 msec were used as in our previous study.[7] The outputs were delivered to the scalp by a single pair of 14.5 mm silver disc electrodes, applied to C3 (anode) and C4 (cathode); (international 10–20 system). Five consecutive stimulations at C3 and C4 were made. The stimulus intensity was set at 700 V.

MEP were recorded from the right APB (the same site as for recording of M-response). Evoked myographic responses were amplified with a 0.3–3 kHz band pass filter and displayed on oscilloscopes (MEB-5508; Nihon Koden, Tokyo, Japan). Experimental MEP study was performed after the induction of anesthesia and before the start of surgery. Peak-to-peak amplitudes and onset latencies were monitored. The mean amplitude and latency were calculated from five consecutive responses to stimulation using a pair of C3–C4 disc electrodes.

The EEG signal was recorded using the Aspect A-1000 EEG monitor (Aspect Medical System, Natick, MA, USA). Silver-silver chloride EEG pads (Zipprep; Aspect Medical Systems) were attached to patient's forehead according to a standard montage.[15] The low - and high - frequency filters were set to 0.25 Hz and 30 Hz, respectively. By ten minutes before the start of surgery, the propofol infusion rate was adjusted to maintain stable BIS score around 50. The propofol infusion rate was not changed thereafter.

To investigate whether MEP to transcranial electrical stimulation under constant blood propofol concentration are affected by arousing effect of surgical noxious stimuli, MEP were collected two minutes before and after the start of surgery. In most cases, approximately 60 min had passed after induction of anesthesia when the first MEP collections were conducted. The start of surgery in this

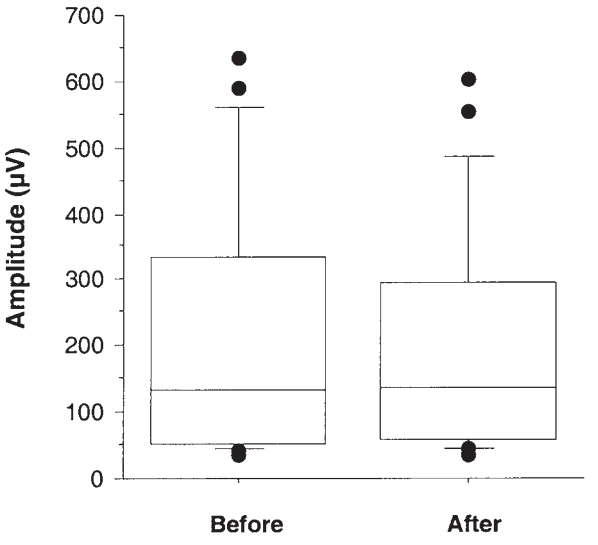

FIGURE 1 Amplitude of motor evoked potentials (MEP) from the right abductor pollicis brevis muscle to transcranial electrical stimulation at stimulus sites of C3–C4 before and after the start of surgery.
Horizontal bars represent the tenth, 25th, median, 75th, and 90th percentiles. One participant was excluded from the analysis because MEP were not elicited (n = 19). Before: two minutes before the start of surgery; after: two minutes after the start of surgery.

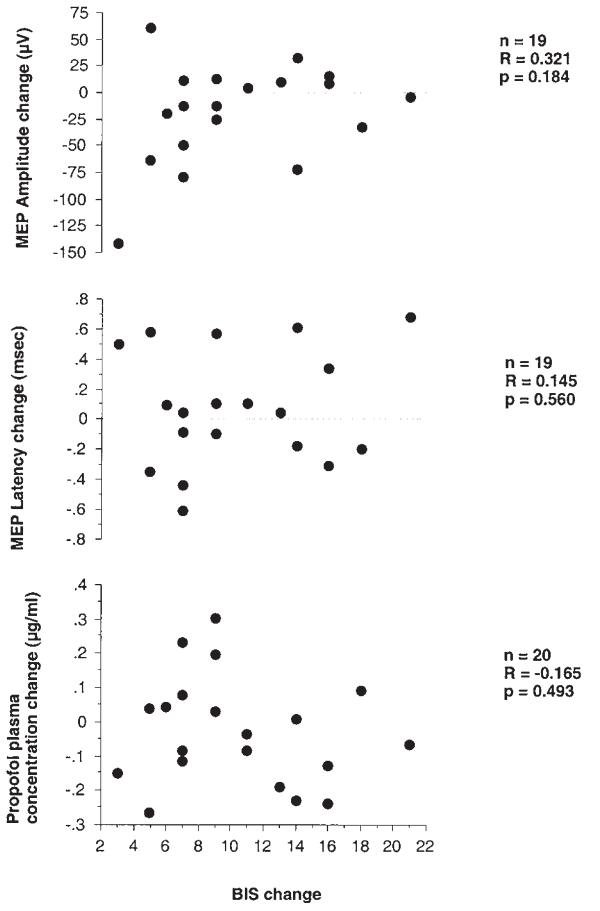

FIGURE 2 Relationships between changes in bispectral index score (BIS) and that of motor evoked potentials (MEP) amplitude and latency, and propofol plasma concentration before and after the start of surgery (n = 19).

study was defined when the initial surgical incision was made. No interventions were made to standardize the degree of stimulation by surgeons because surgical sites were different among patients. At same time points, BIS score, mean arterial pressure (MAP), and heart rate (HR) were recorded and blood samples were collected to confirm that propofol plasma concentration remained constant. Five millilitres of blood were drawn into a heparinized syringe, collected into a glass tube, centrifuged for ten minutes at 3000 rpm, and 2.0 mL of plasma were stored at -20°C for propofol analysis. Plasma concentrations of propofol were determined by high-performance liquid chromatography.

Statistical analysis

Because MEP amplitude-related data did not appear to be distributed normally, they are presented as median, and tenth, 25th, median, 75th, and 90th percentiles. MEP latency-related data are expressed as mean ± SD. A paired t test to compare physiologic variables, BIS score, propofol concentration, and latency of MEP between the two time points, Wilcoxon signed-ranks test was used to compare amplitudes of MEP. The relationships between BIS and MEP amplitude and latency, and propofol concentration before and after the start of surgery were evaluated by Pearson's correlation. Because these values varied with individual patients, especially MEP amplitude and BIS score, the relationships were also analyzed using percent change of these values. Any change of MEP amplitude of more than 50% was defined as a significant modification according to Zhou *et al.*[16] because within- patient variability of MEP, which may lead to a misinterpretation of the MEP, is generally observed.[17,18] Results were considered significant at $P < 0.05$.

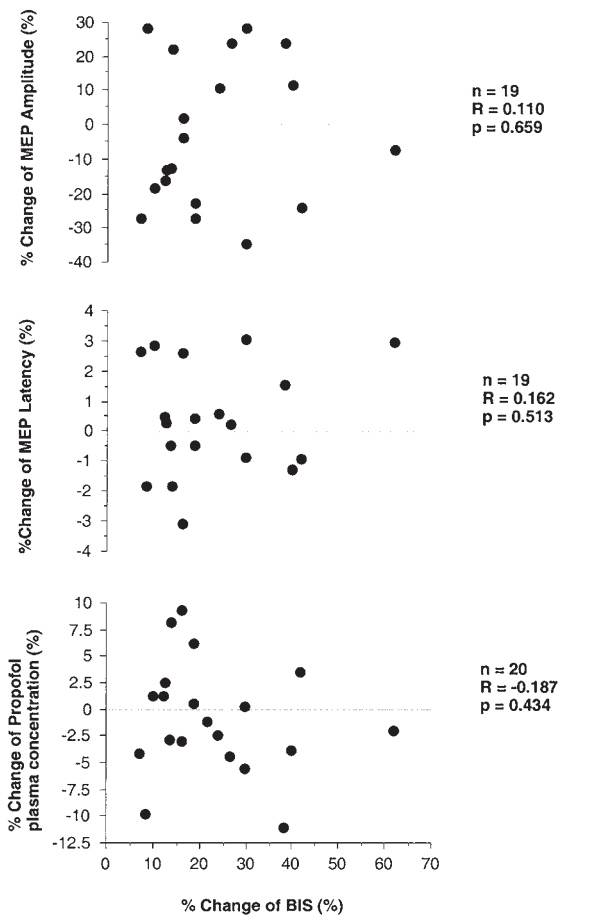

FIGURE 3 Relationships between percent change of bispectral index score (BIS) and that of motor evoked potentials (MEP) amplitude and latency, and propofol plasma concentration before and after the start of surgery (n = 19).

Results

Preoperative motor function was normal in all patients. Their age was 57 ± 19 yr, height 159 ± 9 cm, and weight 55 ± 10 kg (mean ± SD). Disease in the patients included lumbar disc hernia (n = 9), cervical disc hernia (n = 5), ossification of the posterior spinal ligament (n = 3), compression fracture of the lumbar vertebral body (n = 2), and spinal cord tumour (n = 1).

MEP were recorded successfully in all but one patient. MEP peak-to-peak amplitude did not change significantly after the start of surgery (Figure 1) although BIS score did increase significantly (48 ± 6 to 58 ± 5; $P < 0.05$). MEP latency did not change (20.9 ± 1.8 to 20.9 ± 1.9 sec). Plasma propofol concentration was constant (3.3 ± 0.7 to 3.3 ± 0.7 $\mu g \cdot mL^{-1}$). Absolute and percent changes in BIS were not related to changes in MEP latency or amplitude or propofol concentration (Figures 2 and 3). MAP and HR did not change significantly (78 ± 9 to 81 ± 11 mmHg and 63 ± 10 to 67 ± 14 beats·min^{-1}, respectively). No patient showed a significant positive change of MEP amplitude.

Discussion

These results show that noxious stimuli strong enough to change BIS values do not affect MEP to five-pulse transcranial electrical stimulation with a constant plasma propofol concentration. Therefore, we can conclude that MEP can be obtained consistently regardless of anesthetic depth (as evaluated by BIS) if the anesthetic regimen is not changed.

Although a number of authors have reported the effects of anesthetics on MEP induced by motor cortex stimulation, the effect of noxious surgical stimuli on intraoperative MEP monitoring remains unclear. The most plausible explanation for our results is that the effect of an anesthetic on the spinal cord is independent of its supraspinal effects.[19–24] It is likely that synaptic transmission is the primary site at which anesthetics suppress MEP, specifically at the level of the spinal interneuronal or motoneuronal systems.[4] These spinal systems and their evoked potentials do not appear to be affected by the change in anesthetic depth at the supraspinal level. Otherwise, MEP amplification by surgical stimuli might be masked by five-pulse transcranial electrical stimulation, which is an effective way of achieving discharge in a large set of spinal motoneurons. In other words, the amplification by surgical stimuli is only allowed to go so far; however, our study design did not allow the physiology of this response to be determined.

There are several limitations to the study protocol that must be discussed. The effects of different propofol concentrations or BIS scores on our results could be important. In light of ethical concerns, we wanted to avoid higher BIS scores using lower propofol doses. It has been reported that a BIS of 40–55 is usually required during general anesthesia. We targeted a BIS of approximately 50 for this study, which required a plasma propofol concentration of over 3 $\mu g \cdot mL^{-1}$.[11–13] This is recognized as a clinically appropriate concentration and probably higher than those used in other MEP studies.[25] Using a clinically appropriate propofol-based anesthetic, may, possibly, have limited our ability to test our study hypothesis. However, the surgical stimuli appeared to be sufficient to change anesthetic depth even under clinically appropriate propofol-based anesthesia.

The question may also be raised as to whether the anesthetic depth truly changed after the noxious stimuli. The significance of an increase in mean BIS from 48–58 is unclear. The absence of an increase in MAP or HR despite an increase in BIS raises questions about the clinical significance of the BIS increase. Yet, we believe the increase in BIS indicated a change in anesthetic depth, as BIS scores have been reported to be clinically reliable in this assessment.[11–13] Furthermore, BIS increases in response to noxious stimuli prior to or in the absence of hemodynamic or motor reactivity as evidence of inadequate anesthesia in some patients.[26]

Our results support the use of MEP monitoring; however, the response to alterations in anesthetic depth following noxious stimuli remains unclear, creating a dilemma between the need to provide adequate anesthesia and the desire to consistently obtain MEP recordings. It is true that the use of agents that depress MEP or modifications to their concentration in response to noxious stimuli should be avoided. As our results showed, it is also true that anesthetic depth is changed by noxious stimuli during MEP monitoring. Over this decade, methods of intraoperative MEP monitoring have developed greatly, but we should strive to improve the quality of anesthesia during intraoperative MEP monitoring.

In conclusion, we have demonstrated that MEP to transcranial electrical stimulation under a constant and clinically appropriate propofol blood concentration are not affected by surgical noxious stimuli.

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