Monitoring of Immobility to Noxious Stimulation during Sevoflurane Anesthesia Using the Spinal H-reflex

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Background: The spinal H-reflex has been shown to correlate with surgical immobility, *i.e.*, the absence of motor responses to noxious stimulation, during isoflurane anesthesia. Here, the authors established individual concentration–response functions for H-reflex amplitude and tested the predictive power of the H-reflex for movement responses during sevoflurane anesthesia in comparison to electroencephalographic parameters. In addition, they investigated the effect of noxious stimulation on the H-reflex itself.

Methods: The authors studied 12 female patients during sevoflurane anesthesia before surgery. The sevoflurane concentration was increased, a laryngeal mask was inserted, and then the sevoflurane concentration was decreased until H-reflex amplitude (recorded over the soleus muscle) recovered. Thereafter, the end-tidal sevoflurane concentration was kept at a constant value close to the minimum alveolar concentration for suppression of movement responses after tetanic stimulation ($MAC_{tetanus}$), determined by the Dixon up–down method. Pharmacodynamic modeling of H-reflex amplitude and of the Bispectral Index was performed, and predictive values for motor responses to noxious electrical stimulation (50 Hz, 60 mA tetanus, volar forearm) were compared using the prediction probability.

Results: Concentration-dependent depression of H-reflex amplitude by sevoflurane was well modeled (median $r^2 = 0.97$) by a sigmoid function with a median EC_{50} of 1.5 vol% and a median slope parameter of 3.7, much steeper than the slope for the Bispectral Index. $MAC_{tetanus}$ calculated by logistic regression was 1.6 vol%. H-reflex amplitude predicted motor responses to noxious stimulation with a prediction probability of 0.76, whereas the prediction probability for Bispectral Index and spectral edge frequency (SEF_{95}) were not different from chance alone. Noxious stimulation was followed by a substantial increase of H-reflex amplitude for several minutes, whereas the Bispectral Index and SEF_{95} exhibited no significant changes.

Conclusions: Suppression of movement to noxious stimulation and suppression of H-reflex amplitude by sevoflurane follow similar concentration–response functions. Although this does not imply a causal relation, it explains the high predictive value of H-reflex amplitude for motor responses to noxious stimuli, even in a narrow concentration range around the $MAC_{tetanus}$.

THE classic measure of anesthetic potency is the minimum alveolar concentration (MAC) required to prevent 50% of subjects from responding to a noxious stimulus with "gross purposeful movement."[1] Although the suppression of movement is also an important clinical endpoint of general anesthesia, it is a quantal response (all or none) and therefore not useful in the clinical determination of depth of anesthesia.

Aside from the use of physiologic parameters such as heart rate or lacrimation, most attempts to quantify depth of anesthesia have relied on electrophysiologic signals of the forebrain, such as the electroencephalogram or auditory evoked potentials. Derivatives of these signals may correlate well with the sedative component of depth of anesthesia,[2] but they have mostly failed to correlate with immobility (*i.e.*, predicting movement responses).[3-5] This is not surprising, considering the evidence from animal experiments suggesting that anesthetics produce immobility by an effect on the spinal cord. In rats, neither acute precollicular decerebration[6] nor high thoracic spinal cord transection[7] alters the concentration of isoflurane necessary to produce immobility. In a goat model, preferential perfusion of the brain with isoflurane even increased the concentration necessary for immobility.[8,9]

This led to the suggestion that surgical immobility in humans may be monitored using spinal responses such as F waves or the H-reflex.[10,11] The monosynaptic H-reflex was initially described by Hoffmann as a reflex response in the calf muscles after submaximal stimulation of the posterior tibial nerve.[12] The reflex arc includes fast-conducting Ia sensory fibers to the sensory neuron and spinal motoneuron. As early as 1967[13] and then in 1969,[14] the H-reflex had been suggested as a measure of anesthetic depth. More recently, a correlation of H-reflex amplitude and the suppression of movement during isoflurane anesthesia has been reported.[15]

However, to be useful as a monitoring parameter, the predictive value of the H-reflex for movement in response to noxious stimuli has to be evaluated for other anesthetics as well. A parameter indicating anesthetic depth should also be influenced by noxious stimulation itself because depth of anesthesia reflects the balance between nervous system suppression by anesthetic drugs and activation due to surgical stimulation.[16] In addition, the variability of the H-reflex amplitude and its applicability for continuous monitoring need to be assessed.

These issues were addressed in our study in which we recorded H-reflex amplitude continuously (*i.e.*, every 10 s) during anesthesia with changing sevoflurane concentrations and during noxious electrical stimulation at steady state sevoflurane concentrations. Specifically, we

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tested the hypotheses that (1) variability of H-reflex amplitude over time (*i.e.*, between measurements) is low enough to allow for a good correlation with effect compartment concentration and (2) H-reflex amplitude predicts movement responses occurring after noxious tetanic stimulation during sevoflurane anesthesia better than parameters of the processed electroencephalogram.

Materials and Methods

After institutional review board approval (Charité, Berlin, Germany) and written informed consent were obtained, 18 female patients with American Society of Anesthesiologists physical status I or II who were scheduled to undergo elective gynecologic surgery were included in the study. Patient exclusion criteria were pregnancy, diseases affecting the nervous system, use of central nervous system (CNS)–acting medication, abuse of alcohol or illicit drugs, and contraindications for mask induction.

Study Design

The patients were observed before surgery in the anesthesia induction room. Patients fasted at least 6 h before the study and received no premedication. No patient needed or received preoperative pain medication or other CNS-active drugs.

After arrival in the induction room, standard monitoring (noninvasive blood pressure monitoring, electrocardiography, and pulse oximetry) was established, and an intravenous cannula was inserted into a forearm vein. Thereafter, baseline recordings of H-reflex and electroencephalographic parameters were obtained for 10 min before induction. Patients were instructed to keep their eyes closed and refrain from talking and moving during this period.

Anesthesia was induced and maintained with use of sevoflurane *via* a tight-fitting facemask and, after induction, a standard laryngeal mask. Neither opioids nor nitrous oxide was used during the entire study period. End-tidal partial pressure of carbon dioxide (P_{ETCO_2}) was monitored continuously to ensure normocapnia (P_{ETCO_2} 35–40 mmHg) by manual support of respiration. The arterial blood pressure (measured as noninvasive blood pressure) was maintained close to the preanesthetic value with crystalloid and/or colloid infusions. End-tidal sevoflurane concentrations were measured using the infrared spectrophotometric analyzer of an anesthesia workstation (Modulus; Ohmeda, Madison, WI) and recorded in 20-s intervals on a computer disk. A fresh gas flow of 4–6 l/min pure oxygen was used throughout the study period.

Our study protocol comprised two parts for each patient: in the first part, the individual concentration–response function was investigated, and in the second, the response to a noxious electrical stimulus was investigated at steady state sevoflurane concentrations.

To evaluate individual concentration–response characteristics, the end-tidal sevoflurane concentration was steadily increased (starting from zero) until loss of consciousness occurred and insertion of a laryngeal mask was tolerated. After insertion of the laryngeal mask, the sevoflurane concentration was decreased until the H-reflex amplitude showed a marked increase (at least 20% of the difference between baseline value and the value at maximum suppression).

Thereafter, the sevoflurane concentration was kept constant at a value predetermined by the Dixon up–down method.[17] The starting value for the up–down protocol was 1.5 vol%, close to the value reported as the C_{50} for suppression of movement after noxious electrical stimulation.[18] After an equilibration time of 15 min, noxious electrical stimulation (50 Hz, 60 mA, 5 s, 0.2-ms square wave tetanus) was applied *via* a peripheral nerve stimulator (Fisher and Paykel, Auckland, New Zealand) to surface electrodes placed on the volar surface of the forearm. Only gross movements of the head or extremities excluding the stimulated arm were considered positive. After the noxious stimulus, the sevoflurane concentration was kept constant for 5 min. However, after the tetanic stimulus, the experimenter was allowed to terminate the study and increase the sevoflurane concentration *ad libitum* if deemed necessary (rescue medication).

If a positive response occurred (and sevoflurane concentration was not increased as rescue medication), the end-tidal sevoflurane concentration was increased after 5 min by 0.2 vol% (0.3% in the first two patients). After another equilibration period of 15 min, a second noxious stimulus was applied, and the protocol sequence was repeated until no motor reaction occurred.

If no motor response was elicited by the noxious stimulation, the end-tidal sevoflurane concentration was decreased after 5 min by 0.2 vol% (0.3% in the first patient), and the protocol sequence was repeated until a movement response occurred. The study protocol ended when a change in the movement response from positive to negative or *vice versa* occurred. Thereafter, patients received 0.1 mg fentanyl and 0.1 mg/kg cisatracurium before they were intubated and surgery commenced. The starting value of the steady state sevoflurane concentration for the next patient was chosen from the reaction of the previous patient according to the up–down method.

Neurophysiologic Data Aquisition

The H-reflex was evoked and recorded using a Neuropack 4 mini (Nihon Kohden, Tokyo, Japan) machine. Stimulation electrodes were placed 3 cm apart over the posterior tibial nerve at the popliteal fossa, and recording electrodes were placed 10–15 cm apart over the

soleus muscle and the Achilles tendon. All electrodes (including those of the electroencephalograph) were adhesive Ag/AgCl electrodes (Medicotest "blue point"; Istykke, Denmark). Stimuli (0.2-ms square wave) were applied continuously throughout the study with a frequency of 0.1 Hz. The stimulus intensity (mean, 21 mA; range, 8–34 mA) was adjusted to achieve a maximum H-reflex amplitude (30–50% of maximum M wave) before anesthesia induction and was kept constant thereafter. The H-reflex was distinguished from F waves by its recruitment curve and constant appearance. The signal was filtered with a 3-kHz low-pass and a 20-Hz high-pass filter. H-reflex amplitudes were averaged over 30 s for further analysis.

The electroencephalogram was recorded in a bifrontal montage (Fpz-A1 and Fpz-A2) using an A-1000 electroencephalographic monitor (Aspect Medical Systems, Natick, MA). Filter settings were 0.25 and 70 Hz, and the Bispectral Index (BIS) and spectral edge smoothing rates were set to 30 s. Processed electroencephalographic data were recorded *via* a serial communication protocol. The BIS (version B31v02) and the spectral edge frequency at 95% of the power spectrum (SEF_{95}) were used for further analysis. Data from time periods where burst suppression occurred (burst suppression index > 0) were discarded. Electromyographic activity in the frontalis muscle was measured *via* the electrodes of the electroencephalographic monitor.

Data Analysis

Data were screened for changes in M-wave amplitude and shape as a control for constant stimulation and recording conditions. In addition, data with noisy baseline electromyographic activity were excluded, especially during the excitation phase of anesthesia induction.

Individual concentration–response functions were fitted to the data of the first part of the study protocol (until the noxious stimulus) on a spreadsheet program (Excel; Microsoft, Redmond, WA), using a sigmoid model:

$$E = E_0 \times (1 - [c_{eff}^\lambda / \{EC_{50}^\lambda + c_{eff}^\lambda\}])$$

In this model, E_0 is the baseline effect, c_{eff} is the apparent effect site concentration, EC_{50} is the concentration that causes 50% of the maximum effect, and λ describes the slope of the concentration–response relation. The time lag between changes in end-tidal concentration and observed effect was modeled by an effect compartment and a first-order rate constant determining the efflux from the effect compartment k_{e0}.

The relation between end-tidal concentration and the movement response to noxious electrical stimulation was described by the logistic regression model developed by Waud,[19] allowing direct comparison with other concentration–response functions. In addition, the population pharmacodynamic analysis published by Bailey

and Gregg was used. The program Sigmaplot (SPSS version 7.0; SPSS, Muenchen, Germany) was used for these calculations.

To estimate and compare the predictive value of different parameters, we calculated the prediction probability (P_k) introduced by Smith *et al.*[21] P_k is a nonparametric correlation measure that indicates the probability that a parameter correctly predicts anesthetic depth, *i.e.*, in this case, a movement response. A P_k value of 1.0 indicates perfect prediction, whereas a value of 0.5 indicates that the predictive value of the parameter is not better than chance alone. P_k values were compared using a paired-data jackknife analysis.

Logistic regression analysis and the P_k statistic are based on the assumption of independent data. No comparable statistic has been developed that permits dependent data. The assumption of independent data was violated here, as it has been by others,[22–24] because multiple stimuli were applied in each patient. Therefore, SEs may have been underestimated in our analysis.

All other calculations were made using standard statistical software (Prism 3.0; Graphpad Software, San Diego, CA). The influence of noxious electrical stimulation on the H-reflex amplitude itself was evaluated with nonparametric analysis of variance and the Dunn posttest. Values of $P < 0.05$ were considered significant.

Results

Of the 18 patients included, only 12 patients concluded the study. In one patient, no H-reflex could be elicited, and in four patients, the M wave changed during the excitation occurring on anesthesia induction, indicating a shift in electrode position. For another patient, the study had to be terminated because of patient's objection to the tight-fitting mask during anesthesia induction.

Demographic data (mean ± SD) of the 12 patients included in the analysis were an age of 41 ± 11 yr, a body weight of 64 ± 9 kg, and a height of 166 ± 4 cm.

Before anesthesia induction, the measured H-reflexes had an amplitude (mean ± SD) of 4.9 ± 4.0 mV. Induction of anesthesia with sevoflurane led to a gradual decrease in H-reflex amplitude. Latency of the H-reflex and amplitude as well as latency of the M wave remained unchanged. Because of the rapid increase in sevoflurane concentration at the start of induction, loss of consciousness (response to loud and repeated verbal command) occurred on average at 103 ± 25 s (± SD) after starting sevoflurane inhalation. When the sevoflurane concentration decreased, H-reflex amplitude increased again (fig. 1).

The concentration-dependent depression of H-reflex amplitude by sevoflurane could be adequately described by the sigmoid model. Goodness of fit, as judged by r^2 values, was greater than 0.8 in all patients, indicating low
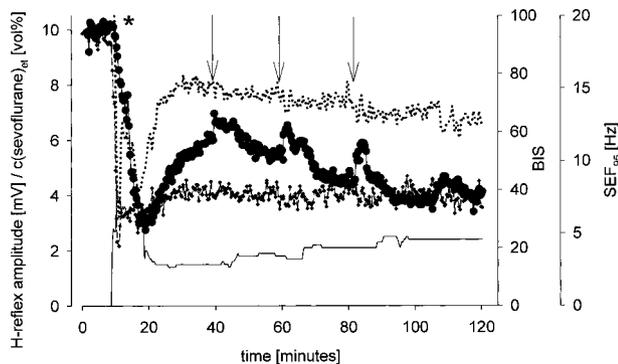
Fig. 1. Time course of an experiment (data from a single patient). After baseline recordings, end-tidal sevoflurane concentration (c(sevoflurane)$_{et}$; *thin line*) was increased until a laryngeal mask was inserted (*asterisk*) and decreased again until the H-reflex recovered. Thereafter, sevoflurane concentration was kept constant for 15 min before tetanic stimulation was applied (*arrows*). After another period of 5 min, sevoflurane concentration was changed according to the motor response. *Connected filled circles* = H-reflex amplitude; *connected diamonds* = Bispectral Index (BIS); *dotted line* = spectral edge frequency (SEF$_{95}$).

variability of the signal. Median values and 25–75% quantiles of the fit parameters are shown in table 1. BIS data were also modeled by a sigmoid model, whereas SEF$_{95}$ data yielded poor fits (median $r^2 < 0.8$; fit parameters are therefore not reported).

The median values for the EC$_{50}$ and the slope parameter were used to construct an average concentration–response curve for H-reflex suppression, which is displayed in figure 2, together with the logistic regression curve for the movement response to noxious electrical stimulation. Logistic regression analysis of the movement response using the method of Waud[19] yielded an
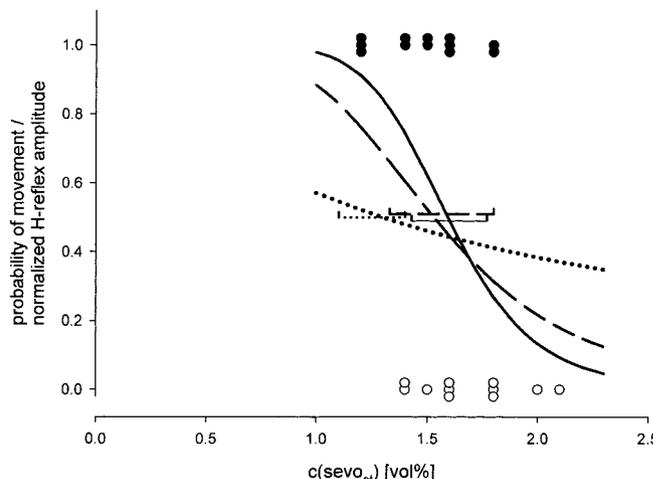
Fig. 2. Comparison of the sigmoid concentration–response curves for suppression of H-reflex amplitude (*dashed line*) and Bispectral Index (*dotted line*) calculated from normalized data of all patients (generated from individual concentration–response curves), and the logistic regression curve for the suppression of the motor response to noxious electrical stimulation (*continuous line*). *Horizontal error bars* = standard errors of the EC$_{50}$ values generated by the computer fits; *circles* = individual movement responses (*filled* = positive response; *open* = no response). H-reflex amplitude has an EC$_{50}$ of 1.5 vol% and a slope parameter of 4.3. Logistic regression of the motor responses yielded an EC$_{50}$ of 1.6 vol% and a steepness coefficient of 8.1 (see Results). c(sevo)$_{et}$ = end-tidal sevoflurane concentration.

EC$_{50}$ of 1.6 vol% (± 0.1 [SE]; 95% confidence interval, 1.43–1.77 vol%) and a steepness coefficient of 8.1 (± 4.3 [SE]). Similar values were obtained when population pharmacodynamic analysis as suggested by Bailey and Gregg[20] was applied, yielding an EC$_{50}$ value of 1.6 vol% and a steepness coefficient λ of 5.6. Therefore, suppression of movement and suppression of the H-reflex by sevoflurane occur in the same concentration range. For comparison, the two concentration–response functions are plotted together in figure 2.

The predictive value of H-reflex amplitude, electromyographic amplitude, BIS, SEF$_{95}$, and end-tidal sevoflurane concentration for the movement response to noxious electrical stimulation was assessed with the prediction probability, shown in table 2. A total of 29 tetanic stimuli were applied, resulting in 15 positive and

Table 1. Pharmacodynamic Parameters of the Sigmoid E$_{max}$ Fits for H-reflex Amplitude and Bispectral Index

	H-reflex	BIS
EC$_{50}$, vol%		
Median	1.5	1.3
25–75% quantile	1.3–1.8	1.2–1.5
k$_{e0}$, min^{-1}		
Median	0.15	0.23
25–75% quantile	0.11–0.18	0.16–0.31
λ		
Median	3.7	1.1
25–75% quantile	2.9–7.3	0.9–1.4
E$_0$, mV/–		
Median	4.9	98
25–75% quantile	4.1–5.0	94–100
r^2		
Median	0.97	0.88
25–75% quantile	0.92–0.98	0.78–0.92

Median values of the fit results from the 12 individual patients and 25–75% quantiles are shown.

BIS = Bispectral Index; E$_0$ = baseline effect; EC$_{50}$ = concentration that causes 50% of the maximum effect; k$_{e0}$ = rate constant determining the efflux from the effect compartment; λ = slope of the concentration–response relation; r^2 = correlation coefficient.

Table 2. Prediction Probability P$_k$ for Movement to Painful Electrical Stimulation for Different Predictors

	P$_k$ Value	SE
H-reflex amplitude	0.76	0.10
End-tidal sevoflurane concentration	0.73	0.10
BIS	0.49	0.12
SEF$_{95}$	0.49	0.11

Prediction probabilities were calculated from reactions to 29 stimuli in a narrow concentration range around the minimum alveolar concentration for suppression of movement responses after tetanic stimulation. SEs were calculated by the jackknife method.

BIS = Bispectral Index; SEF = spectral edge frequency.
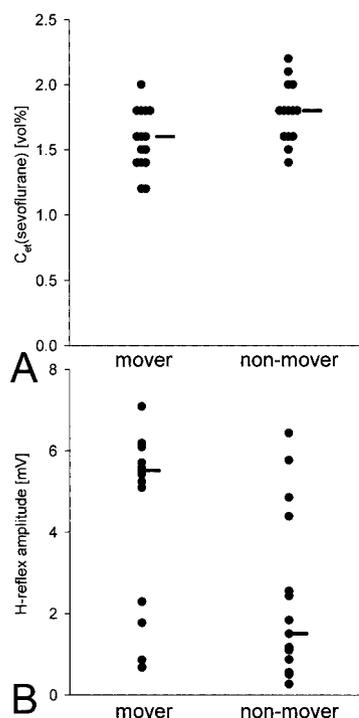
Fig. 3. Individual values for end-tidal sevoflurane concentrations (C_{et}(sevoflurane); *A*) and H-reflex amplitude (*B*) 1 min before noxious electrical stimulation for patients who moved after stimulation (movers; n = 15) and those who did not (nonmovers; n = 14). *Bars* indicate median values.

14 negative responses. Only end-tidal sevoflurane concentration and H-reflex amplitude predicted movement better than chance alone. However, under our experimental conditions, P_k values were low for these parameters, too. A comparison of concentration and amplitude values 1 min before tetanic stimulation for patients who moved (movers) and those who did not (nonmovers) shows overlapping data (fig. 3). P_k values for BIS and SEF_{95} were not significantly different from 0.5. The electromyogram in the frontalis muscle was completely suppressed in all patients before tetanic stimulation; a P_k value was therefore not calculated.

Noxious electrical stimulation at the wrist led to an increase in H-reflex amplitude in the soleus muscle. The mean time course of H-reflex amplitude and other parameters after noxious stimulation is shown in figure 4, excluding data from two patients in whom the sevoflurane concentration was increased because of excessive movement after tetanic stimulation. Tested with nonparametric repeated-measures analysis of variance and Dunn posttest, the increase in H-reflex amplitude (compared to 2 min before stimulation) was significant in the first 3 min. In addition, a trend of larger amplitudes was discernible for more than 5 min. No difference in the response of patients who moved and those who did not was found. For BIS and SEF_{95}, the averaged data from all patients showed no significant increase after noxious stimulation. However, three patients in the mover group
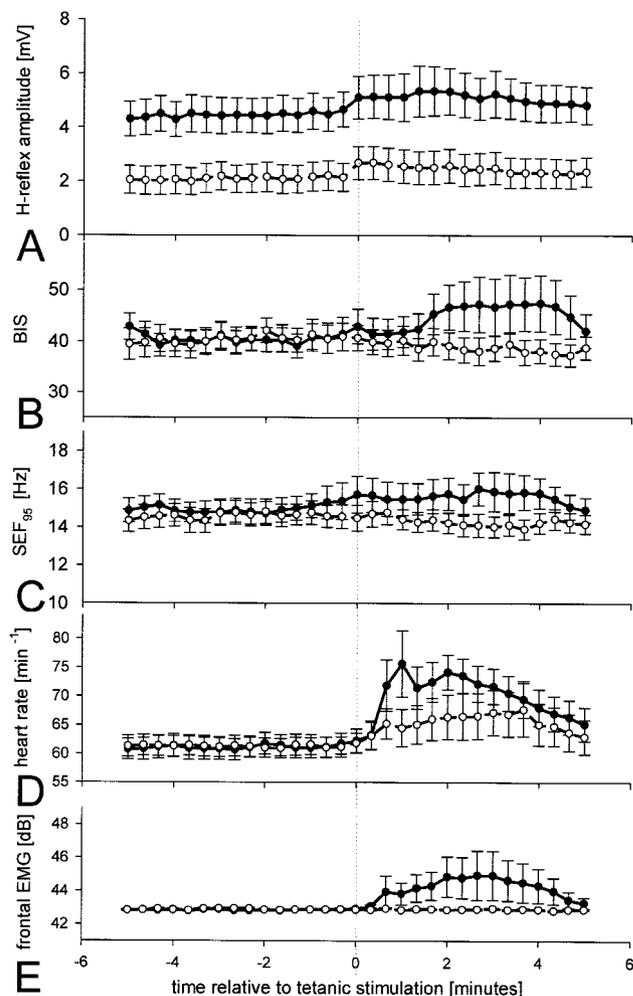
Fig. 4. Response of the different electrophysiologic parameters to noxious tetanic stimulation (at t = 0 min) for patients who moved after stimulation (movers; *filled circles*) and those who did not (nonmovers; *open circles*). Plotted are mean values and SEM for H-reflex amplitude (*A*), Bispectral Index (BIS; *B*), spectral edge frequency (SEF_{95}; *C*), electromyographic activity in the frontalis muscle (*D*), and heart rate (*E*). EMG = electromyograph.

exhibited a marked increase especially in BIS. Electromyographic activity and heart rate increased significantly only for patients with a positive movement response.

Discussion

With this study, it was demonstrated that the concentration-dependent suppression of H-reflex amplitude by sevoflurane could be modeled by a sigmoid concentration–response function. This suppression occurs in the same concentration range as suppression of the movement response to noxious stimulation, with a similar steepness of both concentration–response functions (fig. 2). In contrast, the concentration–response curve for the BIS was shallower (table 1).

Similar concentration–response functions do not nec-

essarily imply a causal connection between suppression of the H-reflex and suppression of the movement response but make H-reflex amplitude a good candidate for monitoring immobility to noxious stimulation. This was confirmed in the performance analysis of predicting movement to noxious electrical stimulation, using the prediction probability P_k. H-reflex amplitude predicts the movement response as well as end-tidal steady state concentration. The absolute values of P_k found in our study were low, most probably because of the narrow spread of sevoflurane concentrations used in our study around and close to the MAC for suppression of movement responses after tetanic stimulation ($MAC_{tetanus}$). When analyzing data spread uniformly in the concentration range of 1.4–2.4 vol%, Katoh et al.[24] have found a P_k of 0.90 for sevoflurane concentration in predicting movement to skin incision. Any measure of correlation, including the prediction probability, takes on higher values when data are sampled further away from the C_{50}.

An additional explanation for the difference between the high P_k reported in the studies of Katoh et al.[24] and the lower value of our study is the steeper concentration–response function for movement in response to skin incision compared to noxious electrical stimulation, as reported by Zbinden et al.[25] for isoflurane. Studies using skin incision as the noxious stimulus should therefore yield higher P_k values. For these reasons, we assume that in our study, we underestimated the predictive value of H-reflex amplitude for prediction of movement to surgical stimuli.

The P_k values for BIS and SEF_{95} were also lower than those found by Katoh et al.,[24] but in both studies, neither BIS nor SEF_{95} predicted movement better than chance alone. In the concentration range of $MAC_{tetanus}$, the concentration–response function of the BIS is shallow (table 1 and fig. 2), and the same has been reported for SEF_{95}.[26] This difference in the steepness of the concentration–response functions may explain the different predictive powers of H-reflex amplitude and the electroencephalographic parameters.

The long-lasting influence of noxious tetanic stimulation on the H-reflex amplitude itself was an unanticipated result of our study. It has been argued that any measure of anesthetic depth should be influenced by surgical stimulation because anesthetic depth reflects the balance between the depressant effects of anesthetics on the CNS and the stimulation of surgery.[16] This shift in the balance between depression and stimulation due to strong stimuli such as abdominal surgery has been shown previously for electroencephalographic parameters[27] and seems to apply also to the H-reflex amplitude. Noxious stimulation, through mechanisms such as temporal summation, may activate spinal circuits to a higher level of alertness. The increased amplitude of the H-reflex might be a reflection of this phenomenon.

It should be noted that in the current study, noxious

electrical stimulation did not lead to an overall change in the electroencephalographic parameters (fig. 4), except in three patients of the mover group, who showed at the lowest concentration a marked increase in the electroencephalographic parameters after stimulation. This is consistent with the literature, in which studies using noxious electrical stimulation have shown no significant change in electroencephalographic parameters,[22] whereas stronger stimuli, such as intubation[28] and surgery,[29] consistently yielded such changes. Therefore, electrical stimulation may lead to spinal arousal without activation of thalamocortical circuits, whereas stronger stimuli are followed by arousal of all levels of the CNS. This is in line with the model that general anesthetics have a dual effect on the CNS: first, they produce unconsciousness by suppression of the forebrain, and second, they block the ascending transmission of nociceptive impulses at the level of the spinal cord or brainstem.[30,31]

Limitations of the Study

The aim of our study was to demonstrate that the H-reflex is suited to monitor surgical immobility, i.e., to predict the motor response to a surgical stimulus such as skin incision. However, instead of skin incision, we used a noxious electrical stimulus. Although studies have shown that noxious electrical stimulation is a supramaximal stimulus in rats, human data have revealed differences in the concentration–response functions of suppression of movement to electrical and surgical stimuli.[25] However, for sevoflurane, the concentration necessary to prevent movement to noxious electrical stimulation in 50% of patients ($MAC_{tetanus}$)[18] has been found to be only slightly lower than necessary to prevent movement to skin incision in 50% of patients.[32] Hence, we assume that our data can be extrapolated to true surgical stimuli and that we probably even underestimated the performance of H-reflex amplitude by using electrical stimulation, because of the shallower concentration–response function for electrical stimulation. It should be kept in mind, however, that tetanic stimulation excites different afferent modalities and that the level of stimulation is substantially less than that of a surgical incision.

Implications of the Study

On a phenomenologic level, our findings imply that the H-reflex can be used as a parameter of the immobilizing effect of sevoflurane. As long as electrode positions are kept constant, continuous monitoring is possible and the predictive value of the signal is reasonably good, as previously discussed. It remains to be determined whether this can be extended also to other groups of anesthetics such as propofol and opioid analgesics. If that were the case, using the H-reflex amplitude would make interaction studies between different anes-

thetics much easier because the H-reflex can be tested with a much higher frequency than the noxious stimulus itself.

On an analytical level, no direct conclusions can be drawn from our data. H-reflex amplitude predicts the movement response as well as the end-tidal steady state concentration, suggesting a close relation between the mechanisms involved in suppression of movement and suppression of the H-reflex. However, the neuronal circuitry responsible for the movement response may nevertheless be different from the neurons and connections involved in the H-reflex. At least in the rat, the force of movement responses to noxious stimuli is not altered by isoflurane until the concentration approaches 1 MAC,[33] whereas the H-reflex was reduced already at much lower concentrations in our study.

As Antognini and Carstens[34] have suggested, the motor reactions to noxious stimulation characterized as "gross purposeful movement" are more complex than a simple reflex twitch. Therefore, an understanding of the mechanisms underlying the suppression of gross purposeful movement to noxious stimulation will ultimately involve the study of anesthetic effects on complex motor processing and not just simple reflexes.

In summary, we have shown that the H-reflex of the soleus muscle can be used for continuous monitoring of immobility to noxious stimulation during sevoflurane anesthesia. However, because H-reflex amplitude is highly sensitive to changes in the exact position of the stimulating electrode, recording of the H-reflex during routine surgery seems to be impractical, at least with the methodology used in our study. In some patients, no H-reflex can be elicited at all. In a study setting, on the other hand, the H-reflex is well suited to assess the immobilizing component of anesthetics in a quantitative manner. Drug interaction studies based on the H-reflex (in comparison to the electroencephalographic or evoked potentials as measures of the sedative component of anesthesia) may then lead to further insights into the mechanisms of anesthesia and the development of guidelines for optimal drug dosing.

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