

Monitoring Sedation Levels by EEG Spectral Analysis

Mark J. Griffiths, MB, BS, FDS, RCS, Alan W. Preece, BSc, PhD,
and Josephine L. Green, BSc

United Bristol Health Trust and University of Bristol Dental Hospital, Bristol, United Kingdom

Real-time electroencephalographic power spectra were obtained for a group of 37 volunteers undergoing sedation with enflurane at different concentrations in air. In part one, 17 subjects were given 0.5%, 0.75%, and 1.0% for 4 min at each level, and recovery after 5 min was assessed by the Trieger method. There was considerable variation in subject response to the different doses, but adequate sedation was indicated by the presence of a strong alpha rhythm (9–11 Hz) and suppression of frequencies below 5 Hz. Overdose was indicated by an initial shift in the alpha frequency to a lower value (6–7 Hz) followed by the appearance of delta waves (0.5–4 Hz) and loss of alpha waves. In part two, 20 volunteers inhaled enflurane at 0.5% for 10 min to allow adequate absorption, followed by a 10-min recovery period. Equal numbers showed sedation or a failure to respond to enflurane at this concentration. In the responders, sedation was accompanied by a marked shift in the ratio of the power in two frequency bands: 1–4 Hz and 8–12 Hz. Progress of the frequency band power ratio followed closely the state of the subject into sedation, overdose, and recovery. This measure was further improved by the use of multivariate analysis, which showed good discrimination of the alert, sedated, and overdosed states of the subject.

In a previous study,¹ we observed that there was no difference between the characteristic electroencephalography (EEG) spectral patterns associated with nitrous oxide (N₂O) conscious sedation and hypnosis. The property of N₂O to enhance the effect of hypnotic suggestion

and vice versa has been exploited in many clinical cases since then, with real-time EEG analysis being used to inform the therapist about the patient's mental state. Improvements in computing technology that made this possible include parallel processing, greatly increased clock speeds, and a reduction in cost by using transputer boards in standard desktop computers.

Enflurane is a volatile agent that has some advantages over N₂O, such as a simpler administration apparatus and easier storage. It has a pleasant ethereal odor that is less pungent and irritating than its analogue, isoflurane. Both agents have been used for sedation and analgesia in obstetrics,² dentistry^{3,4} and intensive care units.⁵

The purpose of this study was threefold: first, to discover whether enflurane can produce EEG effects similar to N₂O or hypnosis; second, to establish the safe maximum sedative dose by observing the dose–response characteristics of the EEG; and third, to use the EEG effects as a model for mathematical discrimination of three states of consciousness, namely alert, sedated, and overdosed/asleep.

METHODS

Ethical Committee approval was obtained to study a total of 37 volunteers (20 male, 17 female) aged 20 to 53 yr (median age 26 yr) in two groups. Excluded were subjects with a history of convulsions, epilepsy, and known psychiatric problems; individuals taking drugs; and women who could be pregnant.

All subjects were monitored for EEG by simple bilateral surface nonadherent silver/silver chloride electrodes in a bipolar configuration linked to a differential amplifier. Electrodes were placed at F₃–O₁ and F₄–O₂ positions (international 10–20 system). Signals were analyzed at a constant gain setting by an analog-to-digital converter and transputer board (Transmed Ltd., Bristol, UK) resident in a desktop computer giving simultaneous data capture, real and processed data display, and storage to disk. Four-sec epochs were refreshed each second without averaging over 0–32 Hz. The power spectrum was derived from a fast Fourier transform (FFT) in near real time.

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Address correspondence to Mark Griffiths, Consultant and Honorary Senior Lecturer in Oral Medicine and Surgery, Bristol Dental Hospital, University of Bristol, Lower Maudlin Street, Bristol BS1 2LY, UK.

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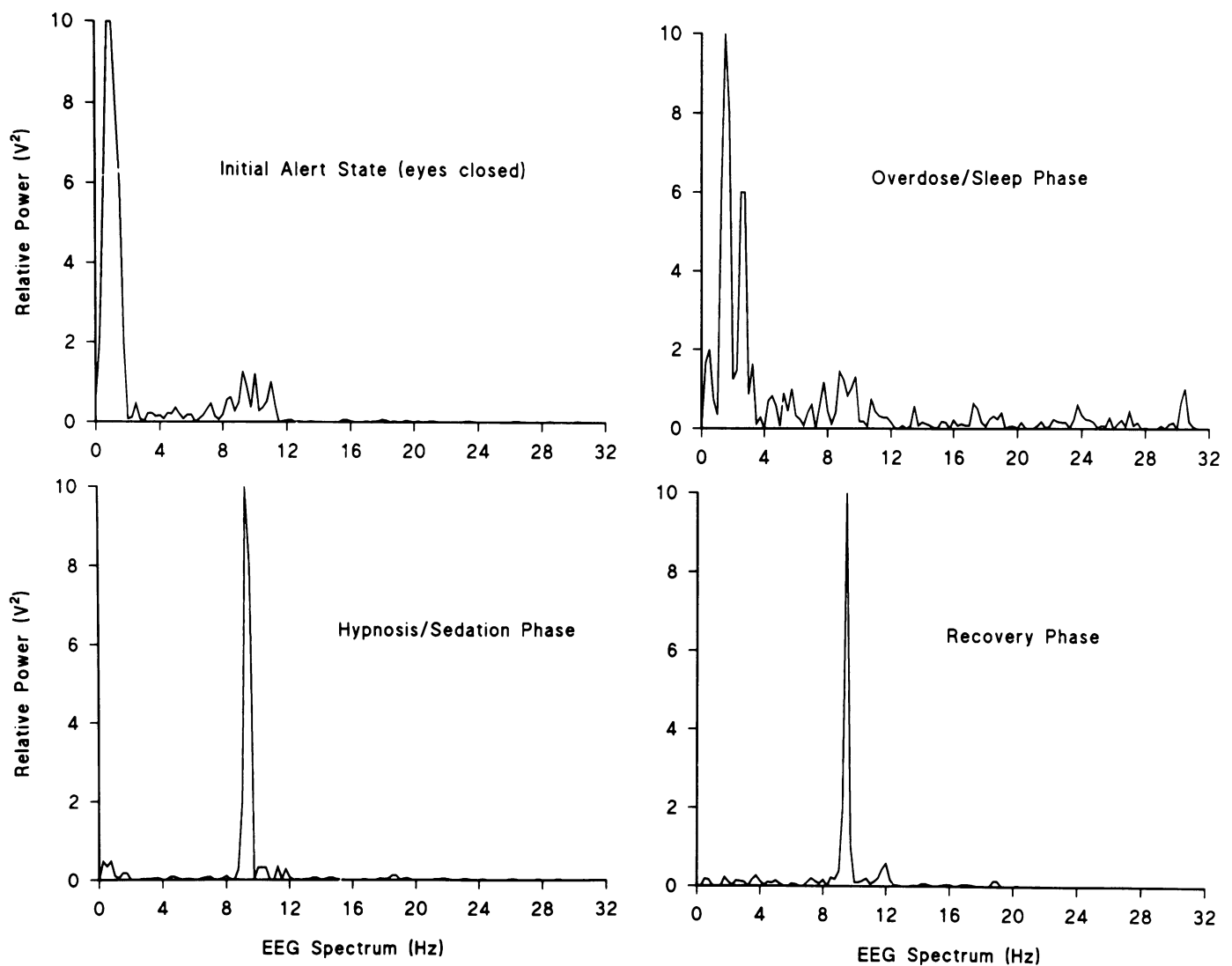


Figure 1. Normalized EEG power spectrum of a single subject inhaling 0.5% enflurane in air. The sequence is from alert, through sedation, to overdose and recovery from overdose.

Enflurane was administered via a nasal mask from a drawover vaporizer. The performance of this device was measured by an Engström Emma monitor (Engström Medical AB, Bromma, Sweden). The first group of 17 subjects was tested at 0.5%, 0.75%, and 1.0% enflurane in air for 4 min at each concentration followed by a 5-min recovery period. The second group of 20 was given 0.5% enflurane for 10 min, followed by 10 min of air alone. Trieger tests⁶ were carried out before and after each administration of enflurane. Pulse oximetry was used throughout. Hypnotic suggestion was avoided, but each volunteer was observed for physical signs of relaxation or sleep. An overdose condition was considered to exist when verbal contact with the subject was lost.⁷

RESULTS

The Trieger test performance of all subjects before and after inhalation of enflurane was analyzed by the Wilcoxon matched-pairs signed-ranks test and showed no significant difference ($P < 0.05$). Pulse oximetry indicated no deterioration in oxygen saturation at any point in the procedure in both groups.

EEG Spectral Analysis

The initial spectrum on eye closure showed considerable variation, in general containing activity in the 0-5 Hz region and a variable amount in the alpha region. Little activity was in evidence above 15 Hz and the study was

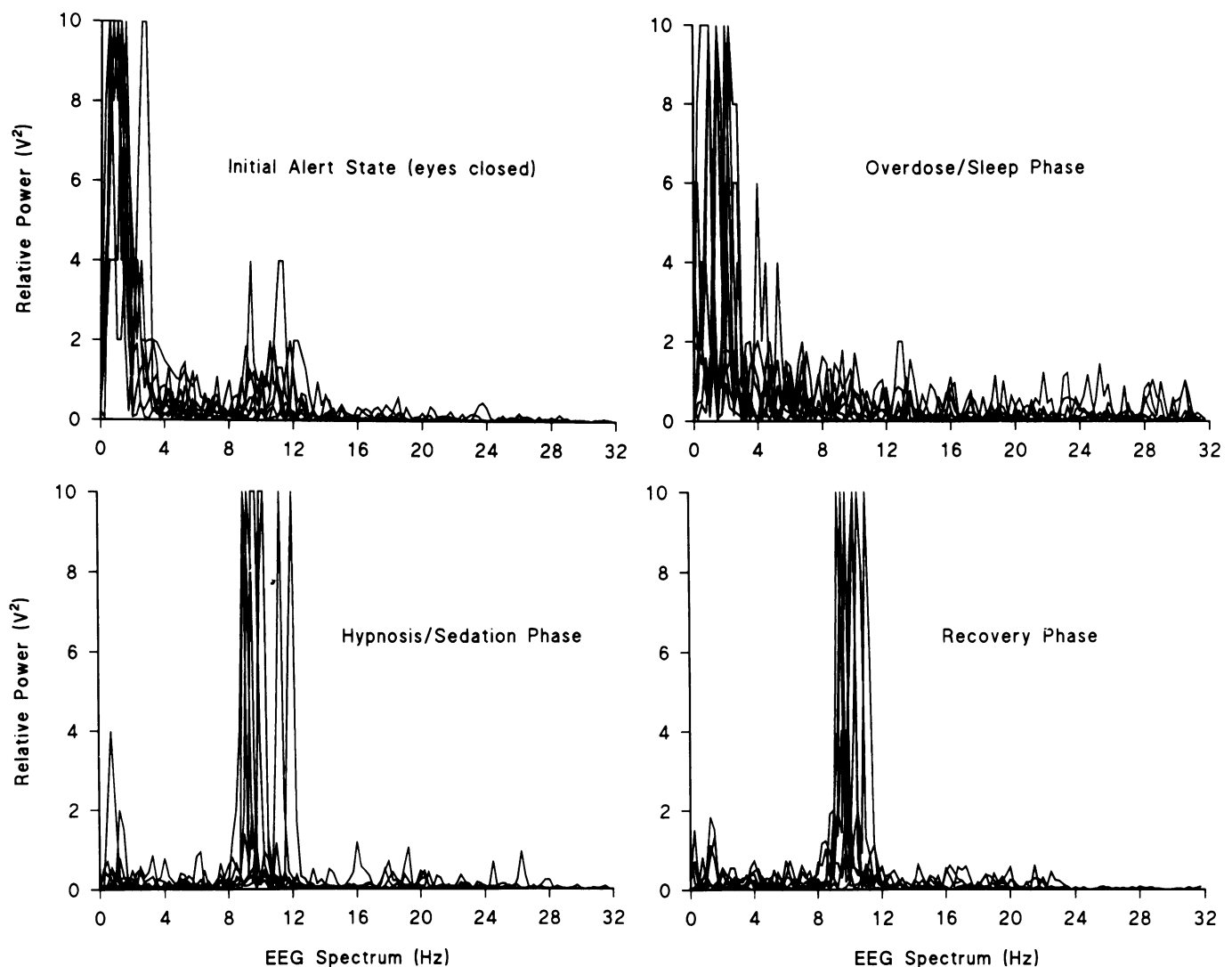


Figure 2. Composite EEGs of eight subjects under the same conditions and sequence as Figure 1 to illustrate the uniformity of response.

limited to 32 Hz. During the progress of inhalation, as the absorbed dose increased, the onset of sedation was associated with a reduction in the 0–5 Hz region and enhancement of the 9–11 Hz region. At this point the EEG spectrum appeared identical to that observed in N_2O conscious sedation and hypnosis, although sometimes new frequencies in the 15 Hz region were detected. At higher doses the alpha rhythm was suppressed and delta (0.5–4 Hz) waves appeared. In some subjects this was preceded by an apparent shift in the alpha frequency to a lower value (6–7 Hz). All subjects showed an alpha rhythm (9–11 Hz) at some stage.

In the first group there was considerable intersubject variation in the response at each concentration. Observation of this group indicated that, for most subjects, concentrations of 0.75% or greater were too high for sedation and 4 min was too little time to achieve equilibration of

the dose of enflurane. The procedure was sometimes cut short because it was clear that verbal contact had been lost and the subject was asleep. For this reason the 20 subjects of the second group were held at 0.5% for 10 min. Ten of these showed no response to the enflurane, and little change in the initial EEG spectrum.

Figure 1 shows a sequence in a single subject from alert, through sedated, to overdosed/asleep, and return to sedation following cessation of the enflurane. Figure 2 is a composite of eight subjects from the 10 responders receiving the second dose regimen and in the same sequence.

Frequency Band Power Ratio Analysis

Calculation of the relative electrical energy in two frequency bands (1–4 Hz and 8–12 Hz) over the course of the procedure is displayed in Figure 3 in the same form

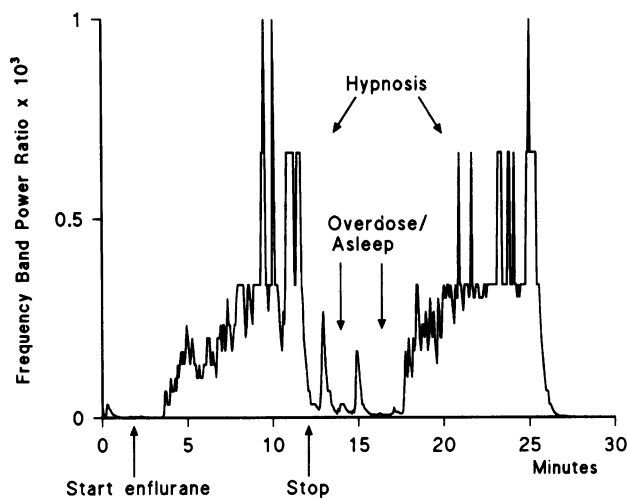
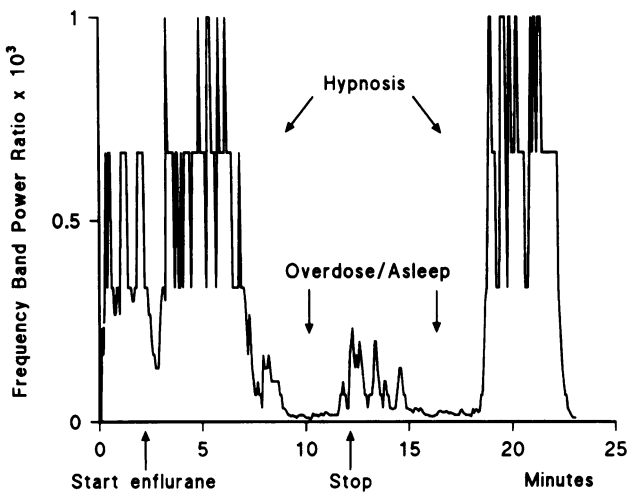


Figure 3. Frequency band power ratio of 1-4 and 8-12 Hz for a "practiced" and relaxed subject (upper trace) and an anxious subject (lower trace) responding to enflurane at 0.5% in air.

as the real-time output to the screen. This is a comparison of two subjects—one of whom was a "practiced" subject, the other a more apprehensive one—and clearly shows that the sedated state is defined by a large increase in the frequency band power ratio. However, the alert state was not separated from the overdose state by this relatively simple analysis, although observation of the "raw data" clearly indicated a decrease in mean amplitude during the overdose period.

Multivariate Analysis

A further method of processing the data is presented in Figure 4. In this case the spectrum derived from the FFT was divided into the 10 percentile frequency bands from

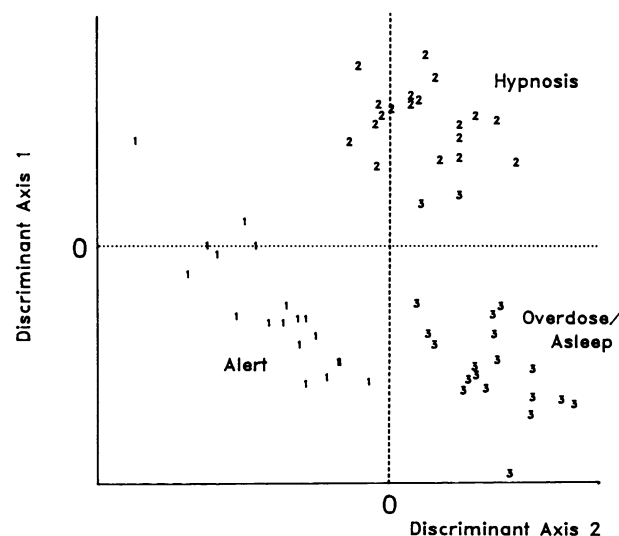
0-32 Hz, which make up nine parameters. Three more were derived from mean frequency, a "zero crossing" count, and a "turns" analysis. Each of these was a signal reversal of more than 1% and was derived from the complex pattern caused by the mixing of the different EEG frequencies. The 12 parameters were combined by the method of multivariate analysis.^{8,9} New discriminant axes were derived from the data such that each axis was a weighted combination of the parameters that best separated the data sets. In this case the three states of the subject were clearly separated into (1) alert, (2) sedated, and (3) overdosed.

DISCUSSION

One of the limitations of the use of a simple desktop computer is that constraints in collecting, processing, and archiving data arise because processes must be sequenced. The approach here of using a separate transputer board for parallel multitasking allowed simultaneous presentation of raw data and processed information to the clinician as well as collection and archiving of data under transputer management. Therefore, the possibility exists of using data in real time to control, for example, the supply of anesthetic/sedative agent, or in a different context, the feedback of information to the subject. Thus, it was important to process the data in a way that avoids ambiguity. This was demonstrated by the use of multivari-

Figure 4. Multivariate analysis of the frequency/amplitude content of the EEG in three subject states (see text for explanation of axes).

MULTIVARIATE ANALYSIS



ate analysis in comparison with a simple analysis of two parameters to produce a frequency band power ratio. The latter did not distinguish the alert from the overdose condition.

The dose of N₂O needed for adequate conscious sedation varies considerably from one individual to another,¹⁰ but control by the clinician is aided by the rapid uptake or elimination of the gas. An additional safety feature is the fact that N₂O has a minimum alveolar concentration (MAC) necessary to achieve anesthesia above 100%, so that when an inspired concentration upper limit of 70% is imposed there is a low risk of unconsciousness. It appears from this study that, for conscious sedation, individual requirements for enflurane also can differ widely. However, the uptake of enflurane is considerably slower than N₂O, and the MAC in oxygen is only 1.9% for young adults. This makes the control of depth of sedation more difficult and inadvertent loss of consciousness more likely. Multivariate analysis of the EEG could provide sufficient early indication of trends to allow safe and accurate titration of the dose of enflurane, and the technique could be applied to other sedative agents.

CONCLUSIONS

This study has shown that (1) enflurane in low doses can produce EEG effects that appear similar to those of N₂O sedation and hypnosis; (2) effective doses for sedation vary markedly between individuals; and (3) multivariate

EEG analysis can produce good discrimination between the alert, sedated, and overdosed/asleep states.

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