Quantitative EEG in assessment of anaesthetic depth: comparative study of methodology†

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Summary

Methodology for assessment of depth of anaesthesia based on analysis of the electroencephalogram (EEG) is controversial. Techniques range from display of single measures, for example median value of the frequency spectrum, to dedicated pattern recognition systems based on measures of several EEG features. We have compared the performance of four techniques using tape-recorded data from 23 patients anaesthetized with either halothane or isoflurane using standardized regimens. The techniques were: (1) median frequency, (2) spectral edge frequency, (3) the cerebral function analysing monitor (CFAM1) and (4) a depth of anaesthesia monitor based on EEG pattern recognition (ADAM). Dose–response curves are presented for stepwise increases in stable end-tidal concentrations of each agent. Results indicated considerable inter-patient variability and the limitations of single EEG measures, particularly with deeper anaesthesia producing a burst suppression pattern in the EEG. Pattern recognition techniques reduced these difficulties and appeared to be promising over a wide range of anaesthetic levels. (Br. J. Anaesth. 1986; 77: 172–178)

Key words

Patients and methods

We were able to use EEG data recorded previously from 23 (ASA I) normotensive patients undergoing elective orthopaedic or gynaecological surgery from the study of Lloyd-Thomas, Cole and Prior [20] during closely controlled, stable, stepwise increases in end-tidal concentrations of either halothane or isoflurane.

The raw EEG data from left and right parietal regions were recorded originally on analogue tape simultaneously with the processing by the CFAM1 monitor [20]. The tapes have now been re-analysed using the ADAM system and comparisons with the original CFAM1 analysis are presented.

After Ethics Committee approval for the original study [20], premedication comprised papaveretum 0.2 mg kg⁻¹ and hyoscine 4 µg kg⁻¹ i.m., 90 min before anaesthesia. This was followed by induction with thiopentone 5 mg kg⁻¹ and fentanyl 5 µg kg⁻¹. Tracheal intubation was performed after tubocurarine 0.5 mg kg⁻¹. Anaesthesia was maintained with either isoflurane or halothane and 66 % nitrous oxide in oxygen.
oxide in oxygen. End-tidal carbon dioxide was maintained at 5 %. If systolic arterial pressure decreased to less than 100 mm Hg, anaesthesia was lightened, and data from that part of the recording rejected from analysis, to avoid any possibility of unwanted effects of hypotension.

Twelve patients received isoflurane at end-tidal concentrations of 0.5, 1.0, 1.5 and 2.0 vol % and 11 patients received halothane at end-tidal concentrations of 0.5, 1.0 and 1.5 vol %. Artefact-free samples of 5 min duration were obtained during the control period with nitrous oxide in oxygen after a stabilization period of 15–20 min at each end-tidal concentration of the volatile agent and during recovery.

**SIGNAL PROCESSING**

The paper traces of the original unprocessed EEG were used to select artefact-free samples corresponding precisely to the marked periods analysed in the original study [20]. These were studied with the following methods of analysis.

**Median and spectral edge frequencies**

Median (MF) and spectral edge (SEF) frequencies were calculated as the 50th and 95th centiles of the accumulated value of the EEG power spectrum using the integrated frequency analysis in the ADAM system (fig. 1) based on 10th order auto-regressive modelling.

**Cerebral function analysing monitor (CF:AM1)**

After passage through an asymmetric band-pass filter, EEG amplitude and frequency were analysed digitally. The results were stored as numerical data and plotted on a screen and on paper. The clinician interpreted the charted results of analysis against an unprocessed EEG display when required. Amplitude and its variations were displayed as the mean, 90th and 10th centiles and maxima and minima outside these values. Frequency analysis using a modified zero-crossing technique, indicated every 2 s the percentage of the total energy falling into the following bands: beta2 (>20 Hz), beta1 (14.3–20 Hz), alpha2 (10–14.3 Hz), alpha1 (7.7–10 Hz), theta2 (5.3–7.7 Hz), theta1 (3.5–5.3 Hz), delta2 (2.0–3.5 Hz), delta1 (1–2 Hz) and very low frequency (<1 Hz), together with separate detection of percent time with EEG suppression (<3 μV RMS).

For this study the results of CF:AM1 digital analysis of 2-s segments of the EEG were obtained from the previous work on the same tape-recorded data [20]. In addition, a “fast/slow EEG frequency ratio” was calculated: (beta2 + beta1 + alpha2 + alpha1)/(theta2 + theta1 + delta2 + delta1).

**Advanced depth of anaesthesia monitor (ADAM)**

This system was based on a pattern recognition system which uses calculations of probabilities derived from previously studied normal reference distributions of EEG from patients receiving iso-flurane and halothane at different concentrations [17–19]. Contiguous 2-s periods of the EEG were passed through a filter which first, limited low-frequency components likely to be artefactual and second, counteracted the inherent skewed frequency/amplitude distribution of the EEG. The features extracted from each sample represented both spectral distribution and amplitude of the EEG. The system was trained by a pattern processing technique (unsupervised repetitive hierarchical cluster analysis) to produce a set of reference patterns for halothane and isoflurane [17–19]. Within each set the individual patterns were grouped and assigned colours to represent specific depths of anaesthesia so providing a simple “anaesthetic scale” divided into six levels: “drowsy” (dark blue), “very light” (light blue), “light” (green), “normal surgical” (yellow), “deep” (purple) and “very deep” (red) anaesthesia. Awake states, artefacts and movements were assigned to the “background colour” of the display. This colour coding bypassed the problem of interpreting agent-specific data, in that the same overall scale was displayed for the equivalent ranges even though the EEG patterns from which it was derived were different for each agent.

Both the class probability histograms (distribution of recognized reference EEG patterns) and the simultaneous colour-coded density spectral arrays (EEG frequency distribution) were plotted with a time resolution of 10 s, each point displayed on the chart being based on a weighted average over the immediately preceding period (approximately 30 s). EEG suppression was detected separately using a method based on time domain descriptors over 0.25-s periods. This enabled us to modify the original pattern recognition so that 2-s periods with suppressions of 0.25–0.75 s were assigned to “normal anaesthesia”, those with suppression of 0.75–1.25 s to “deep anaesthesia” and those with suppression of 1.25–2.00 s to “very deep anaesthesia”. To facilitate comparison with other monitoring techniques, the class probability histograms were converted to a single numerical value representing the depth of anaesthesia such that the value 6.0 represented “very deep” anaesthesia and 1.0 represented “drowsy”. A value for anaesthetic depth was then calculated for each 10 s.

**STATISTICAL ANALYSIS**

An unpaired two-tailed *t* test was performed on the group data for each step in end-tidal concentration of each anaesthetic, that is control period nitrous oxide vs 0.5 % end-tidal concentration of inhaled anaesthetic, +0.5 % vs +1.0 %, etc. and +1.5 % or +2.0 % vs “recovery”.

All group data are presented as dose–response curves of the digital values from the various monitor outputs and derived variables against the end-tidal concentrations of the volatile agents, and data are displayed as mean (sd). The significance of the change in mean value compared with the previous state is given above the second of each pair using the following notation: *P* < 0.01, **P* < 0.001, ***P* < 0.0001; symbols in parentheses indicate significant
changes in the opposite direction to the overall trend for each variable (e.g. increased MF/SEF for increased anaesthetic depth).

**Results**

**ISOFLURANE**

The group data for MF (fig. 2) showed considerable inter-patient variability but this was less evident with increasing depth of anaesthesia up to an end-tidal concentration of 1.5%. From 1.5% to 2.0% there was no further change in MF. In contrast, the corresponding curve for SEF (fig. 3) did not exhibit a clear trend and inter-patient variability was high. Significant changes (decrease in SEF) were seen only from pure nitrous oxide in oxygen to 0.5% and from there to 1% end-tidal isoflurane concentration. With higher concentrations (+1.5%) SEF began to increase but thereafter (+2.0%) no further change occurred.

The CFAM1 amplitude data (fig. 4) replicated Bickford’s 1950 work [5] showing an initial increase with light levels of anaesthesia and then a progressive decrease with increased depth of anaesthesia until burst suppression occurred. There was considerable variability in the CFAM1 group data and the only single frequency measures showing a continuous (but not significant for each step at \( P < 0.01 \)) trend with increased depth of anaesthesia were theta1 and beta1. The calculated fast/slow ratio (fig. 5) based on the group data from the CFAM1 showed a clear trend up to +1.0% end-tidal concentration. However, a further increase produced only a small decrease in the fast-slow ratio. None the less, seen as group data this ratio did not, in contrast with other single EEG measures, reverse at +2.0% when two-thirds of patients developed burst suppression. Inter-patient variability was considerable, although it can only be indicated by the “standard deviation” bars shown in figure 5. Note that the standard

![Figure 1: An example of power spectral analysis of an EEG segment during isoflurane anaesthesia. The spectral distribution was calculated using an autoregressive model of the 10th order. Each of the traditional single EEG measures, median frequency (MF) and spectral edge frequency (SEF), was derived from this curve, being the 50th and 95th centiles of the accumulated power value of the EEG frequency spectrum.](image)

![Figure 2: Median frequency; group data showing dose–response curves for patients receiving isoflurane (n = 12, left) and halothane (n = 11, right). The graphs show mean (SD) values during the sequence: nitrous oxide in oxygen (N₂O + O₂), step-wise increases in end-tidal concentration of the volatile agent and during recovery (R). The significance of changes in mean values (based on unpaired two-tailed \( t \) tests) compared with the previous state is given above the second of each pair using the following notation: *\( P < 0.01\); **\( P < 0.001\); ***\( P < 0.0001\); symbols in parentheses indicate significant changes in the opposite direction to the overall trend for each variable (e.g. increased MF for increased anaesthetic depth).](image)
deviations are not legitimate for these CFAM1 group data as the frequency measures are based on pooled individual data and thereby not independent observations, and therefore no significance values could be calculated.

With the ADAM system (fig. 6), the group data showed highly significant and consistent trends with increasing end-tidal isoflurane concentrations, even though inter-patient variability was marked.

With most individual patients there was a clear initial decrease in MF towards deeper levels of anaesthesia with a relative low intra-patient variability. However, with increasing end-tidal concentrations of isoflurane from 1.5 to 2.0 %, MF showed a non-linear relationship in almost 50 % of patients, paradoxically suggesting “lightening” anaesthesia. Such patients all exhibited burst suppression patterns in the unprocessed EEG at an end-tidal isoflurane concentration of 2.0 % or, in some, even at 1.5 %. The corresponding SEF curves showed a poor correlation with increase in the end-tidal concentration. The spurious appearance of lightening of anaesthesia again occurred with burst suppression. Few of the individual curves produced a clear trend and inter-patient variability was high compared with the relatively small overall changes in SEF. Intra-patient variability was low, as with MF, but with small overall changes between different

Figure 3  Spectral edge frequency (SEF); group data showing dose–response curves for patients receiving isoflurane (n = 12, left) and halothane (n = 11, right). Layout and symbols as in figure 2.

Figure 4  CFAM amplitude (top) and suppression (bottom); group data showing dose–response curves for patients receiving isoflurane (n = 12, left) and halothane (n = 11, right). Layout and symbols as in figure 2. CFAM1 amplitude values (peak-to-peak) are mean (○) and 90th and 10th centiles (∗).
anaesthetic concentrations. The CFAM1 showed, in all except one patient, an initial increase in amplitude with light levels of anaesthesia and then a progressive decrease with increasing end-tidal concentrations until onset of burst suppression. However, four patients not exhibiting burst suppression did not produce any further decrease in CFAM1 amplitude for 1.5 and 2.0 % end-tidal concentrations. Intra-patient variability for CFAM1 amplitude was relatively low except during burst suppression, however, there was a considerable spread in absolute amplitude values between patients, indicating difficulties in producing a reliable measure of anaesthetic depth based solely on this feature.

The CFAM1 frequency measures showed marked intra- and inter-patient differences and the only consistent results were seen for beta1 + 2 and theta1 bands. EEG activity in the entire beta frequency band seemed significantly suppressed for moderate to deep levels of anaesthesia, but inter-patient variability for light levels was quite high. In most patients the theta1 band showed a clear trend to increase with increasing end-tidal concentrations. The calculated fast/slow ratio based on the pooled individual data from the CFAM1 decreased with end-tidal isoflurane concentrations up to 1 % but in the majority of patients a further increase in end-tidal concentration produced only minor changes. For three patients an initial increase was seen in the fast/slow ratio comparable with that in the CFAM1 amplitude measures. In four patients there was a small increase in the fast/slow ratio during burst suppression at 2.0 % end-tidal isoflurane. ADAM, the pattern-recognition system, showed consistent and uniform dose–response curves to approximately 1.5 % in all except three patients with relatively low intra- and inter-patient variability. In these three patients the dose–response curve flattened just before short suppressions first appeared in the raw EEG, indicating difficulties in detection of the first signs of discontinuity in the EEG.

HALOTHANE

The group data for MF (fig. 2) showed inconsistency in trend and high inter-patient variability, even though changes for each step increase in halothane concentration were significant. The corresponding values for SEF (fig. 3) decreased progressively with increased end-tidal concentrations, but the changes for the first step (nitrous oxide in oxygen to +0.5 %) were significant only at $P < 0.01$. The CFAM1
amplitude measures (fig. 4) showed only a non-significant trend with increasing halothane concentration and no EEG suppressions were detected in any patient. All CFAM1 frequency measures showed considerable variability as in the isoflurane study. The only frequency variables indicating a consistent trend with increased depth of anaesthesia were beta1 + 2 and, to a limited degree, theta1. However, although beta1 changed significantly ($P < 0.01$) for the first two steps, individual traces were variable. The calculated CFAM1 fast/slow ratio (fig. 5) showed a trend similar to MF, but the variability in EEG frequency changes with halothane reduced the potential value of this ratio. In contrast, the ADAM system (fig. 6) gave a near-linear relation with end-tidal concentration of halothane for group data but tended to overestimate the depth of anaesthesia for pure nitrous oxide in oxygen because of inconsistent initial changes in three patients (see below).

In individual patients, neither MF nor SEF produced a consistent trend with increasing end-tidal halothane concentrations. In four of 11 patients there was a decrease in MF and SEF after the period of nitrous oxide in oxygen alone, but it should be noted that inter-patient variability was considerable. Of the individual CFAM1 measures, none showed any significant trend with increased end-tidal concentration except for beta1 + 2 which, for all but two patients, appeared markedly suppressed for end-tidal concentrations of $+1.5\%$ or above. The individual CFAM1 amplitude dose–response curves were very variable with no consistent trend. No uniform pattern was evident with any of the CFAM1 frequency variables except theta1 which, in five of the patients increased with increasing end-tidal concentration. After an initial variable increase, the fast/slow ratio decreased in all patients with end-tidal concentrations greater than $+1.5\%$. With the ADAM system there were more consistent trends but inter-patient variability was marked, especially compared with the isoflurane study. For three of the 11 patients, the ADAM system wrongly assessed pure nitrous oxide in oxygen effects as representing deeper anaesthesia than during $+0.5\%$ end-tidal concentration of halothane. A similar problem occurred in six patients for MF and in four for SEF.

**Discussion**

We have compared the performance of four different techniques for assessment of depth of anaesthesia with the volatile agents isoflurane and halothane using the same set of tape-recorded data obtained in a previous study [20]. As in other studies it was evident that methods using a single EEG feature are inadequate over the range of anaesthetic depths which include EEG burst suppression pattern [6, 12].

The CFAM1 had the advantage of displaying multiple features so that the user could identify individual changes with alterations in end-tidal concentration and, importantly, immediately recognize the burst suppression pattern. In addition to indicating deep anaesthesia, this pattern may have serious implications (e.g. hypoxia or ischaemia). However, it requires experience to learn the overall CFAM pattern combinations for each anaesthetic and with the launch of each new agent, further patterns would have to be assimilated. These considerations appear to have been addressed in a new version (CFAM3) about which preliminary information has been made available [personal communication, D. E. Maynard, 1995]. The development of the ADAM system uses a different approach where an unsupervised clustering technique is used to define a reference set of naturally occurring EEG patterns for different types and depths of anaesthesia. These reference patterns are then used in on-line pattern recognition during anaesthesia to display a simple-to-interpret, anaesthetic depth indicator. As yet the data base is relatively small and limited to the anaesthetic techniques on which it has been trained. We are presently completing studies to extend the anaesthetic database and on detection of changes caused by other aspects or complications of surgery and anaesthesia (asymmetries of any variables, distinction between deep anaesthesia, hypothermia and hypoxic–ischaemic complications).

The two examples of single EEG feature methods which we have investigated, MF and SEF, failed to characterize deepening anaesthesia when the burst suppression pattern had appeared in the EEG. Typically this EEG pattern was seen when end-tidal isoflurane concentrations were in the range $+1.5$ to $+2.0\%$. This problem of burst suppression pattern in the EEG has not been addressed adequately by previous authors who have recommended single feature methods (MF or SEF) on the basis of studies on a previous study [20]. As in other studies it was evident that methods using a single EEG feature are inadequate over the range of anaesthetic depths which include EEG burst suppression pattern [6, 12]. Indeed some possibility of misclassification still exists with the ADAM system during early burst suppression. It should be noted that the CFAM1, in spite of the above mentioned problems regarding the complexity of a multivariate display, does clearly indicate even very early burst suppression patterns.

The limitations of single EEG measures for monitoring depth of anaesthesia have been indicated by others [6, 12] but the approach of using a pattern recognition system based on multiple features has received only limited attention [17–19] and has not previously been subjected to comparative studies. On the evidence of the results we believe it would be fruitful to explore such systems further. The techniques appear to have the potential of overcoming many of the difficulties previously associated with EEG monitoring of depth of anaesthesia. Moreover, on theoretical and practical grounds they are likely to be more generally applicable than methods based on evoked potential monitoring. Evoked potentials provide a crucially important tool for assessment of integrity of neural pathways during some spinal and intracranial surgical procedures. However, they require a skilled operator and their value for assessing anaesthetic depth in an individual patient appears to apply mainly to the lighter levels of anaesthesia.
Only when a highly reliable measure of depth of anaesthesia can be obtained in an individual patient will we achieve the aim of clinical acceptability.

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References