Auditory steady-state response, upper facial EMG, EEG and heart rate as predictors of movement during isoflurane-nitrous oxide anaesthesia

A. YLI-HANKALA, H. L. EDMONDS JR, M. F. HEINE, T. STRICKLAND JR AND K. TSUEDA

SUMMARY
We have studied the relationship between patient movement and changes in the auditory steady-state evoked potential, upper facial muscle electromyogram (FEMG), electroencephalographic-zero crossing frequency (EEG-ZCF) and heart rate during emergence from anaesthesia. Twelve healthy patients underwent surgery during stable isoflurane-nitrous oxide-oxygen anaesthesia without neuromuscular block. After skin closure, anaesthesia was discontinued abruptly while mechanical ventilation was continued until the patient moved. The magnitude of change in each physiological signal was evaluated in decibels (dB). Both the auditory steady state evoked potential and FEMG showed significant increases in amplitude during the last 5-min period before movement (6.1 and 10.7 dB, respectively). EEG-ZCF increased rapidly after anaesthesia was discontinued (2.5 dB) but there was no further increase in activity before movement. Heart rate did not change before movement. The use of the decibel transformation offers a promising method of displaying and interpreting changes in physiological variables during anaesthesia. (Br. J. Anaesth. 1994; 73: 174-179)

KEY WORDS

Adequacy of anaesthesia is estimated usually by changes in the autonomic nervous system assessed clinically. However, these signs may be unreliable in predicting responsiveness during surgery [1-3]. Recently, objective methods of monitoring adequacy of anaesthesia have been introduced. Quantitative electroencephalographic methods have been advocated as indices of anaesthetic depth [4, 5]. Electromyographic activity of upper facial muscle (FEMG) has been shown to increase during inadequate anaesthesia [6, 7]. Middle latency auditory evoked potentials have shown dose-related changes with anaesthesia [8-10] and are thought to predict movement [11] and demonstrate awareness [12] during anaesthesia. A comparative study of these variables has not been reported.

This study was designed to evaluate physiological signals during emergence from anaesthesia, that is in a situation where inadequate anaesthesia is produced intentionally. We studied the relationships between movement and changes in the steady state auditory evoked potential, upper FEMG, electroencephalographic-zero crossing frequency (EEG-ZCF) and heart rate during emergence from standardized isoflurane-nitrous oxide anaesthesia in patients.

PATIENTS AND METHODS
After obtaining local Ethics Committee approval and informed consent, we studied 12 ASA I or II patients (table I).

Auditory steady state response
A Cadwell Quantum 84 (Cadwell Laboratories, Kennewick, WA, USA) evoked potential device was used for acoustic stimulation and recording of evoked potentials. Rarefaction clicks of 0.1 ms and 50 dB above the normal hearing level were presented to the patients binaurally via headphones at a rate of 39.8 Hz. For recording, gold-plated cup electrodes were positioned at the vertex and left earlobe with an extracephalic ground. Inter-electrode impedances were maintained less than 5.0 kΩ and the...
amplification bandpass was set at 10–100 Hz. The auditory response (one average of 100 epochs) was recorded before induction of anaesthesia. Ten averages of 1000 epochs were recorded during the last 15 min of surgery. After discontinuation of anaesthesia, the evoked potential was averaged once every 1 min (typically 600–700 epochs) until the first spontaneous movements (coughing, grimacing or movement of arms or legs) of the patient were seen. Amplitudes of the auditory responses were measured off-line. 

**FEMG, EEG and heart rate**

Upper FEMG and EEG were measured by an AMB2 (Datex/Instrumentarium, Helsinki, Finland). Biopotentials recorded with surface electrodes were pre-amplified, portions of the full bandwidth selectively filtered (1.5–25 Hz bandwidth (±3 dB) for the EEG and 65–300 Hz for the FEMG) and quantified. Mean integrated voltage of the FEMG and EEG-ZCF were determined. Heart rate was recorded continuously with a Datex Cardiocap (Datex/Instrumentarium). Digitized values for these three measures were obtained at 10-s intervals and stored in comma-delimited ASCII format. Recordings began before induction of anaesthesia and were continued until the first spontaneous movements after anaesthesia.

**Anaesthesia**

Midazolam 1–2 mg i.v. was given 20 min before induction of anaesthesia. Anaesthesia was induced with thiopentone 5 mg kg⁻¹. Tracheal intubation was facilitated with suxamethonium, but no other neuromuscular blocking agents were given. The lungs were ventilated mechanically (end-tidal carbon dioxide concentration was maintained at 5.0%). Anaesthesia was maintained with isoflurane and 60% nitrous oxide in oxygen. Nasopharyngeal temperature was measured. Clinically appropriate end-tidal concentration of isoflurane was adjusted to a level sufficient to render the patient immobile but maintain systolic arterial pressure > 90 mm Hg. Thereafter, isoflurane concentration was maintained constant to the end of anaesthesia, monitored by a Datex Capnomac monitor. Bolus doses of fentanyl 50 μg were given if necessary to manage tachycardia, arterial pressures greater than awake levels or movements during the early phase of operation. After skin closure, isoflurane and nitrous oxide were discontinued abruptly. Mechanical ventilation (FiO₂ 1) continued without touching the patient until the first spontaneous movements were seen. Except for continuously testing the auditory evoked response, no other auditory stimuli were presented to the patient. The operating room was kept quiet during emergence from anaesthesia.

**Statistical analyses**

Comparison of changes in various indices is difficult because of the different units. A decibel (dB) transformation with individualized baselines makes the indices directly comparable on a common scale. Thus data from each variable were transformed to decibels for each patient separately:

\[
dB \text{ change from baseline} = \left( \frac{\text{log (current value/baseline)}}{10} \right) \times 10
\]

Baseline for the auditory steady state evoked potential was determined from the mean amplitude of 10 intraoperative recordings during the last 15 min of operation. Baselines for EEG, FEMG and heart rate were obtained for the same times as those for testing of auditory evoked potentials. The baseline was the mean of the 10-s median values. The medians were used because of skewing over the measurement interval. Values for each 1 min during the last 5 min preceding movement were compared with the baseline values to evaluate change. In each case the a priori hypothesis tested was that a positive change in the adequacy measure would occur in time-related fashion after discontinuation of an-

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**Table II. Mean (95% confidence limits) steady-state auditory evoked potential (AEP), upper facial muscle EM (FEMG), EEG zero-crossing frequency (EEG-ZCF) and heart rate (HR) before induction of anaesthesia, during steady-state anaesthesia and during the last 1 min before movement**

<table>
<thead>
<tr>
<th></th>
<th>Before induction</th>
<th>During surgery</th>
<th>Last 1 min before movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEP (μV)</td>
<td>1.91 (0.78, 3.04)</td>
<td>0.24 (0.19, 0.28)</td>
<td>1.15 (0.34, 1.96)</td>
</tr>
<tr>
<td>FEMG (μV)</td>
<td>3.41 (2.81, 4.01)</td>
<td>0.15 (0.06, 0.24)</td>
<td>3.0 (1.05, 4.95)</td>
</tr>
<tr>
<td>EEG-ZCF (Hz)</td>
<td>7.9 (6.52, 9.28)</td>
<td>5.36 (4.77, 5.95)</td>
<td>9.78 (8.28, 11.28)</td>
</tr>
<tr>
<td>HR (beat min⁻¹)</td>
<td>79.4 (66.4, 92.4)</td>
<td>79.0 (69.2, 88.8)</td>
<td>82.0 (72.7, 91.3)</td>
</tr>
</tbody>
</table>

**Table III. Mean (95% confidence limits) decibel-transformed values of FEMG, EEG-ZCF and HR during surgery (baseline) and before movement. **P < 0.01 compared with baseline (ANOVA and Dunnett’s multiple comparison test)**

<table>
<thead>
<tr>
<th>Time before movement (min)</th>
<th>Baseline</th>
<th>-5</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMG</td>
<td>-0.09</td>
<td>1.79</td>
<td>2.34</td>
<td>4.07</td>
<td>5.25</td>
<td>10.7**</td>
</tr>
<tr>
<td></td>
<td>(0.33, 0.15)</td>
<td>(0.16, 5.26)</td>
<td>(0.06, 5.74)</td>
<td>(-0.14, 8.28)</td>
<td>(0.56, 9.94)</td>
<td>(6.2, 15.19)</td>
</tr>
<tr>
<td>EEG-ZCF</td>
<td>-0.02</td>
<td>1.91**</td>
<td>1.92**</td>
<td>2.56**</td>
<td>2.23**</td>
<td>2.54**</td>
</tr>
<tr>
<td></td>
<td>(-0.11, 0.08)</td>
<td>(0.95, 2.87)</td>
<td>(1.00, 2.84)</td>
<td>(1.54, 3.17)</td>
<td>(1.24, 3.22)</td>
<td>(1.61, 3.47)</td>
</tr>
<tr>
<td>HR</td>
<td>0.00</td>
<td>-0.13</td>
<td>-0.10</td>
<td>-0.07</td>
<td>-0.08</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>(-0.03, 0.03)</td>
<td>(-0.39, 0.13)</td>
<td>(-0.29, 0.09)</td>
<td>(-0.28, 0.15)</td>
<td>(-0.31, 0.14)</td>
<td>(-0.2, 0.44)</td>
</tr>
</tbody>
</table>
operation, movement responses appeared in 10.8
not given during the last 30 min of anaesthesia. After
Fentanyl was
1
0.91 (95 % confidence limits 0.82, 1.0) %. Mean total
figures 1-3. Table II shows the results as raw data,
The results are presented in tables II and III and in
movements. Statistical significance was accepted
analysis of variance, followed by Dunnett's multiple-
range test. Regression analysis was performed be-
istically significant change at least 1 min before
muscle EMG (FEMG), amplitude of 40-Hz steady-state auditory
heart rate (HR) during emergence from anaesthesia (see fig. 1).
We have found that after discontinuation of stable
transiently (from 5.5 to 7.5 Hz).
EEG—ZCF decreased after induction (table II) and increased rapidly after discontinuation of an-
We have found that after discontinuation of stable
EEG—ZCF reached its maximum within
min. Heart rate remained essentially unchanged
during and after anaesthesia (table II, fig. 2).
One patient moved during operation in response
to surgical stimulus. This movement was predicted
1.5 min earlier by an increase in the amplitude of the
FEMG (from 0.09 to 4.7 μV). An increase was seen
also in the amplitude of the auditory evoked potential
(from 0.44 to 1.73 μV) and in heart rate (from 55 to
96 beat min−1). There was no change in EEG—ZCF
until the patient moved, when EEG—ZCF increased
transiently (from 5.5 to 7.5 Hz).

DISCUSSION
We have found that after discontinuation of stable
isoflurane—nitrous oxide anaesthesia, the amplitudes
of both the auditory steady-state evoked response
and the FEMG increased and patient movement
could be predicted by each of these indices.
EEG—ZCF increased rapidly after discontinuation of anaesthesia but did not change further during the
last 5 min before movement. Heart rate did not
change before movement.
The auditory steady-state response is produced by
repetitive auditory stimuli (clicks or tone bursts) at a
rate of approximately 40 Hz [13]. The resultant
sinusoidal evoked waveform represents the middle
latency range of auditory responses. The amplitude
of the response has been shown to reflect the level of
alertness or arousal [14] and is reduced greatly
during anaesthesia [15, 16]. In our study, the
amplitude of the auditory steady-state evoked response
remained low during anaesthesia and then,
after discontinuation of anaesthesia, continued to
increase up to the time when patients moved
spontaneously. These findings support the view that
middle latency auditory evoked response may be
valuable for predicting movement.
The origin of upper facial muscles is visceral [17].
aesthseia. A reliable measure would show a
statistically significant change at least 1 min before
movement. Data were analysed using one-way
analysis of variance, followed by Dunnett's multiple-
range test. Regression analysis was performed be-
tween the anaesthetic doses and time delay in
movements. Statistical significance was accepted
when P < 0.05.

RESULTS
The results are presented in tables II and III and in
figures 1–3. Table II shows the results as raw data,
that is before decibel transformation.
Mean steady-state isoflurane concentration was
0.91 (95 % confidence limits 0.82, 1.0) %. Mean total
fentanyl dose was 2.4 (1.8, 3.0) μg kg−1. Fentanyl was
not given during the last 30 min of anaesthesia. After
operation, movement responses appeared in 10.8
(6.5, 15.1) min (range 4–23 min) after discontinu-
ation of anaesthesia. Mean end-tidal isoflurane
concentration at the time of movement was 0.23
(0.16, 0.30) %. The time delay from discontinuation
of anaesthesia to movement did not correlate with
the amount of fentanyl (P = 0.25), the length of
anaesthesia (P = 0.08) or the isoflurane steady-state
concentration (P = 0.54). Nasopharyngeal tempera-
ture decreased by less than 0.4 °C in all subjects.
No patient had spontaneous conscious recall or
dreams related to intraoperative events during
anaesthesia.

The amplitude of the 40-Hz auditory steady-state
response decreased after induction of anaesthesia. It
increased again before movement (table II, figs 1–3).
The amplitude of the upper FEMG also decreased
after induction of anaesthesia. It remained stable
during surgery and increased typically 1–3 min
before movement (tables II and III, figs 2 and 3).
EEG—ZCF decreased after induction (table II)
and increased rapidly after discontinuation of ana-
esthesia. However, after the initial abrupt increase,
no further increase in EEG—ZCF occurred until the
time of movement (table III, fig. 2). In a patient who
did not move until 23 min after discontinuation of
anaesthesia, EEG—ZCF reached its maximum within
4 min. Heart rate remained essentially unchanged
during and after anaesthesia (table II, fig. 2).

FIG. 1. Steady-state 40-Hz auditory evoked potential (AEP)
during and after anaesthesia in 12 patients (mean (SD)). Each value
is an average of the recording during the 1 min at the time marked.
Values are decibel transformations representing the change from
baseline values recorded during stable anaesthesia. Shaded area =
95 % confidence limits (CL); — — = upper 95 % CL during
steady-state anaesthesia. **P < 0.01 between baseline values and
measurements during emergence from anaesthesia.

FIG. 2. Lower 95 % confidence limits (CL) amplitude of facial
muscle EMG (FEMG), amplitude of 40-Hz steady-state auditory
evoked potential (AEP), EEG—zero crossing frequency (EEG) and
heart rate (HR) during emergence from anaesthesia (see fig. 1).
- - - = 0 dB, representing approximately the upper 95 % CL of
recordings during anaesthesia.
Their motor innervation arises from the brainstem, with connections to vigilance centres in the reticular formation. Thus the upper FEMG has been used to monitor the adequacy of anaesthesia [6, 7, 18, 19]. However, this method has not gained wide clinical acceptance, probably because inter-individual variability in the amplitude of the FEMG may limit its use [20]. We also found great variability in FEMG amplitude between patients during anaesthesia. The amplitude, however, increased markedly, shortly before movement. The increase in amplitude was most conspicuous during the last 1 min. Thus the FEMG appears to be a sensitive method of predicting movement.

No single “gold standard” for adequate anaesthesia has been derived from the EEG [21, 22]. Most intraoperative EEG studies have measured the effect of drugs on cortical electrical activity rather than the subcortical processes that help to determine adequacy of anaesthesia [23]. No correlation was found between quantitative EEG measures and the adequacy of anaesthesia in rats [24]. Responsiveness to external stimuli is controlled by subcortical structures of the brain [25], but the subcortical activities are not generally reflected in the surface EEG. In our patients, a stepwise increase in EEG-ZCF occurred after abrupt discontinuation of anaesthesia. After that there was no further significant change in EEG-ZCF during the last 5 min of emergence from anaesthesia. The initial increase was probably caused by the rapidly decreased cortical concentrations of isoflurane and nitrous oxide, a drug combination that slows the EEG [26, 27]. It was not associated with returning of responsiveness. The present study suggests that EEG-ZCF does not predict movement during emergence from anaesthesia.

Changes in heart rate and arterial pressure are mediated by autonomic reflexes, which are also under the control of the hypothalamus. Some fibres of the pain-transmitting spinothalamic tract terminate in the hypothalamus [28]. There are also rich connections between the hypothalamus and the limbic system. Anaesthetics and adjuvants may affect these areas in several incompletely understood ways. These observations may explain the fact that many previous reports have shown the unreliability of clinical signs in monitoring the adequacy of anaesthesia [1–3].

We used a decibel transformation to make all indices directly comparable. The individualized baseline provided a useful measure of change for each patient. The logarithmic transformation inherent in the decibel measure reduced the skewness of the data and thus made a more appropriate choice for parametric statistical analysis than percentage change. The use of confidence limits gives an estimate of change: with $n > 10$, absence of overlap between two confidence limits indicated that the sample means differed at the specified level of confidence [29]. The 95% confidence limit spanning zero in the heart rate data indicated that the mean baseline value and that from each 1-min sample before movement came from the same population, that is no significant change at $P < 0.05$.

Both the low pass filtered EEG and high pass filtered EMG signals were derived from the complex biopotential recorded from the frontomastoid electrode pair. With two active electrodes, the EMG signal is a composite of upper facial and postauricular muscle activities. However, the sudden large increase in EMG amplitude observed typically on emergence from anaesthesia may be attributed primarily to the facial muscles, as postauricular auditory evoked responses (PAER) may remain intact during sleep [30]. Repetitive acoustic stimulation at 40 Hz leads to superimposition of rhythmical middle latency auditory evoked potentials with a period of 25 ms. As this latency is similar to that of the PAER, postauricular muscle contamination of the 40-Hz response is a possibility. However, persistence of the PAER during somnolence makes such contamination unlikely. Furthermore, the PAER is optimally obtained with an active electrode on the mastoid. Thus our use of the earlobe for recording the steady state response minimized the influence of the PAER.
Several studies have documented the relative insensitivity of the upper facial muscles to non-depolarizing neuromuscular block [31, 32]. These muscles remain responsive even when the electrically evoked thenar EMG response has been depressed by 90% from pre-block baseline values [7]. Such patients would be judged clinically to be completely relaxed, because all signs of mechanical thumb twitch are abolished at 75-80% depression of the evoked EMG response. Therefore, continuous monitoring of the FEMG appears to provide a simple and reliable method for detection of inadequate anaesthesia, provided that excessive neuromuscular block is avoided.

We made our measurements during emergence from anaesthesia. Patients moved as a response to the tracheal tube, rather than surgical stimulation. Thus our data should be extrapolated with caution in evaluating the adequacy of anaesthesia during surgery. One of our patients moved during steady-state anaesthesia and surgery. The EEG-ZCF showed no change in this patient. However, this event was preceded by an increase in both auditory evoked potential and FEMG amplitude, suggesting that these indices may be useful as indicators of inadequate anaesthesia during surgery.

In summary, we have evaluated the usefulness of auditory steady-state evoked potential, upper FEMG, EEG-ZCF and heart rate as predictors of movement during emergence from isoflurane anaesthesia. Our data suggest that movement may be predicted best by the measures of subcortical function rather than cortical or autonomic nervous system-mediated functions. The use of the decibel transformation with confidence limits offers a promising method of displaying and interpreting comparative changes in physiological measurements during anaesthesia.

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REFERENCES

