Age-related changes in EEG power spectra in infants during sevoflurane wash-out

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Editor’s key points

- Changes in the electroencephalogram (EEG) could signal emergence from anaesthesia in infants, but few data are available.
- During wash-out of sevoflurane, infants >3 months old had higher power in the 5–20 Hz range, which decreased before awakening.
- This change in the EEG might be a useful predictor of emergence in titrating anaesthesia in older infants.

Background. Few electroencephalography (EEG) data are available in anaesthetized infants. This study aimed to identify EEG characteristics that might warn of awakening (AW) from sevoflurane anaesthesia in infants.

Methods. Twenty intubated infants [aged 39–77 weeks post-menstrual age (PMA)] were studied after surgery during sevoflurane wash-out. EEG was recorded at the end of surgery and throughout emergence. Changes in EEG time and frequency domains were described.

Results. At the end of surgery, mean end-tidal sevoflurane concentration was 2.3% (range 1.5–3.5) before wash-out and reduced to 0.3% (0.1–0.6) when AW began. On AW, movement artifacts made signals difficult to interpret. Before awakening, most power was within frequencies ≤4 Hz, but trends over time were variable. Summated power in frequencies between 20 and 70 Hz was almost always <5 μV². During anaesthesia, there were two common power spectra: infants >52 weeks PMA had obvious summated power in the frequency range 5–20 Hz (P5–20 Hz) (mean 308, median 320, range 110–542 μV²), which decreased before awakening began [mean decrease 252 μV² (95% CI 153–351)], whereas younger infants had low P5–20 Hz throughout. P5–20 Hz during anaesthesia increased with age; power in this frequency band of ~100 μV² separated infants younger and older than 52 weeks PMA.

Conclusions. During sevoflurane wash-out, decreasing P5–20 Hz might warn of impending AW in infants >3 months old, but not in younger infants.

Keywords: anaesthesia, general; consciousness monitors; electroencephalography; infant; sevoflurane

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An assessment of the effect of anaesthetic agents on the depth of anaesthesia is important in infants as in older patients. If, in order to avoid excess anaesthesia, the dose is minimized, it would be desirable to have a monitor of anaesthesia depth that could warn of unintended awakening (AW). Electroencephalography (EEG), including monitors of processed EEG, might be suitable but few data are available in anaesthetized infants.1 The data from adults might not be applicable because EEG characteristics in infants are known to differ from those in adults.2

In their review of EEG in children, Constant and Sabourdin2 state that, typically, a sedative dose (or concentration) of sevoflurane increases beta activity and as the dose increases to cause anaesthesia, high-amplitude low-frequency oscillations appear. If the dose is increased further, there is EEG suppression with intermittent bursts (burst suppression) followed by EEG silence. EEG changes during sevoflurane wash-out and emergence are assumed to be the same but in reverse. The evidence, however, for these changes occurring in infants is limited. There are four published data sets of EEG effects of sevoflurane in infants and small children: one during induction, two during emergence, and one during surgery.

Induction was studied by Constant and colleagues3 in children aged 2–12 yr. An increase in dose was associated with an increase in total spectral power especially in low-frequency bands, and 14–30 Hz oscillations were common.

Of the emergence data sets, Davidson and colleagues4 studied toddlers and children (anaesthesia also involved opioids and some had isoflurane), and Lo and colleagues5 studied children aged 22 days to 3.6 yr emerging from either sevoflurane or isoflurane alone. Both studies found that during steady-state anaesthesia, infants <6 months old have low...
EEG changes during sevoflurane wash-out in infants

EEG power, but in older infants, as in adults, there is appreciable power in frequencies between 2 and 30 Hz. However, their observations on EEG changes associated with emergence conflict. In one study, the power within the 2–20 Hz range decreased, and in the other, power within the 8–30 Hz range increased.

Hayashi and colleagues studied processed EEG variables in 62 neonates and infants having surgery (some had fentanyl and a caudal block) during steady sevoflurane concentrations between 0.5 and 2%. In children aged 6 months to 2 yr, spectral edge frequency (SEF90) was inversely related to sevoflurane concentration, but this was less so in younger infants. Below ~3–5 months of age, the SEF90 was always low.

We studied the EEG, both in time (i.e. visual appearance of the ‘raw signal’) and frequency domains, in infants during emergence from sevoflurane to determine characteristics that could be used to warn of potential AW. In a pilot study before this project, infants would frequently remain immobile during wash-out unless they were stimulated and then often awaken suddenly. This has been observed by others. We considered that it was necessary to provoke AW and therefore needed a stimulus that could be repeated without causing distress. During natural sleep in infants, McNamara and colleagues showed that tickling the foot caused a reproducible sequence of AW behaviour. First there was a withdrawal response of that limb, then a change in heart rate or breathing pattern, followed by a startle and EEG responses coincident with AW. These may relate to activation of the spinal reflex, then the brain stem, followed by the sub-cortical nuclei and finally the cerebral cortex.

This observational study describes the changes in the EEG of infants during wash-out of sevoflurane with AW provoked by gentle cutaneous stimulation.

Methods

The project had ethical committee approval and parents gave written informed consent. Infants (aged < 12 months) requiring anaesthesia involving tracheal intubation were recruited unless they had any cerebral, cardiac, or respiratory disorder or were receiving any medication likely to affect neurological function. Post-menstrual age (PMA), body weight, and relevant clinical details were recorded.

Anaesthesia was not altered for this study and was induced and maintained by sevoflurane; nitrous oxide was not used for maintenance. Monitoring included pulse oximetry, electrocardiography (ECG), respiratory gas analysis, and non-invasive arterial pressure. Tracheal intubation was achieved after muscle relaxation with atracurium. Anaesthetic gases were administered via a circle breathing system. Inspired sevoflurane was adjusted to maintain end-tidal concentrations considered compatible with adequate depth of anaesthesia according to the clinical judgement of the anaesthetist. Ventilation was controlled to maintain end-tidal carbon dioxide concentration between 3.5 and 5.5 kPa (respiratory rates were ~20 min⁻¹ and the end-tidal capnograph waveform had a recognizable plateau).

Analgesia varied and was achieved with combinations of local anaesthesia (levobupivacaine 0.25%) and other potent analgesics (i.e. fentanyl or morphine). All infants received i.v. fluids in volumes guided by the clinical judgement of the anaesthetist who assessed heart rate, arterial pressure, and skin perfusion to ensure that infants were not hypovolaemic or dehydrated. Body temperature was maintained > 35.5 °C. No antimuscarinic drugs were used. Atracurium was not reversed with neostigmine because > 1 h had passed between emergence and the last dose. After surgery, the inspired concentration of sevoflurane remained unchanged from that used during surgery for at least 1 min. Sevoflurane administration was then stopped and washed out with fresh gas flow of 8 litre min⁻¹. Mechanical ventilation was unchanged until effective spontaneous breathing started. End-tidal sevoflurane concentration (PetSevoflurane) was recorded every minute until tracheal extubation.

Observations and recordings were made and taken by M.R.J.S. who was not involved with administering the anaesthetic. From ceasing sevoflurane administration until AW (wash-out period), AW was provoked by two types of stimuli. The sole of the foot was continuously stroked with a plastic 20 g i.v. catheter. If the infant had a caudal epidural local anaesthetic block, a hand was stroked instead. A standard arterial pressure measurement caused stimulation by its cuff inflation once every minute. The cuff, placed on the arm, automatically inflated to a maximum pressure of ~ 100 mm Hg and inflation lasted ~ 30–40 s. Ambient noise was unrestricted and normal for an operating theatre environment.

Video recording enabled timing of events: sevoflurane turned off (SO), first movement of a limb (M1), awakening began (AB), AW, and tracheal extubation. AW was defined as the presence of at least two of five criteria (crying or attempting to cry, vigorous limb movements, gagging on a tracheal tube, eyes open, and looking around). AB was defined as the first occurrence of one criterion. A brief single movement of a limb in response to tickling was not a criterion of AW. EEG signals were divided into epochs of 6 s. Timing of events was recorded in seconds, converted into the nearest epoch, and then converted into ‘decimal minutes’ (e.g. 6.2 decimal minutes = 6 min and 12 s). Behavioural changes could be subtle and consequently the timing of an event might have been no more precise than ± 1 epoch.

EEG signals were recorded from silver/silver chloride cup electrodes placed on the scalp with electrolyte paste and adhesive tape. Electrode impedance was < 5 kΩ. Two frontal (F3 and F4) and two centro-parietal (CP3 and CP4) electrodes were referenced to the bridge of the nose. A Grass-Telefactor Twin ‘AURA 10–20’ (Natus Neurology Incorporated, Grass Products, Warwick, RI) multi-channel recording system (version 3.7.85.0) was used to acquire signals in the range of 0.3–70 Hz and sampled at 400 Hz.

EEG recordings were analysed off-line. Sequences of emergence EEG up to 24 min were prepared for analysis in each patient starting from 1 min before sevoflurane was turned off until full AW. Raw EEG signals were visually inspected and their (time domain) characteristics were described in...
terms of frequencies and amplitudes of oscillations. Signals were then analysed using bespoke MATLAB® programmes incorporating a Discrete Fourier Transform algorithm (version 7) (software developed by MathWorks, MA). Epochs were not analysed if there was appreciable interference or transient activity (see Appendix). Power spectrum density (PSD) was estimated for each epoch by the Welch method. Frequency resolution was 1 Hz. Power (μV²) was calculated for conventional EEG frequency bands: 1–4 (delta), 4–8 (theta), 8–13 (alpha), 13–30 (beta), and 30–70 (gamma) Hz. In order to provide greater precision of changes in the frequency spectrum, power was also calculated within narrower frequency bands: 1, 2–4, 5–8, 9–12, 13–16, 17–20, 21–24, and 25–28 Hz.

Band powers in frontal and centro-parietal channels during anaesthesia were calculated. The channel with the largest mean power within the 1–28 Hz band for the whole patient group was chosen for further analysis. The mean EEG power spectrum and mean band powers (mean of 10 epochs in both left and right channels) were calculated for two 1 min periods after surgery: before sevoflurane was turned off (bSO) and immediately before awakening began (bAB). Band powers in these two periods were compared. Data were log10 transformed if the mean and median were dissimilar. Differences between means were supported by 95% confidence intervals. Where differences were appreciable, the variable was calculated for every epoch during the emergence sequence and plotted to identify any trend. Regression described trend over time. Logistic regression was used to test and measure association of a change in any band power with age and other factors.

Results
Parents of 35 infants were approached and 20 consented. Infant ages ranged from 39 to 77 weeks PMA (Table 1). All except one moved the same limb that was being stroked before any other behaviour or obvious change in heart rate or respiratory pattern. In the exceptional infant, there was a generalized motor response that preceded AB by one epoch. Arterial pressure cuff inflation did not appear to have a time relationship to movement or AW.

There was a wide variation in AW times. Time between SO and AW ranged from 6.2 to 36.3 min. AB was always at least 5 min after SO. Movements were always vigorous and M1 was at least 1 min before AB. Four infants moved almost immediately on the first stroke but then took 7.5, 8.2, 10, and 14.5 min until AB. Six infants took <1 min between AB and AW. The youngest infants took the longest to AB, but there were no obvious relationships between age and event time.

Before SO the mean PetSevoflurane was 2.3% [standard deviation (SD) 0.5, range 1.5–3.5] and there was no relationship to age. During wash-out, there was a rapid decrease in PetSevoflurane in the first minute but thereafter it decreased slowly. The mean PetSevoflurane was 0.5% by 5 min (SD 0.1, range 0.3–0.8) and 0.4% by 7 min after SO (SD 0.1, range 0.3–0.7). At AB, the mean PetSevoflurane was 0.3% (SD 0.1, range 0.1–0.6).

During wash-out, the raw EEG signal had two easily distinguishable periods: before AB, there was almost artifact-free activity but during AW, there was EMG interference and artifact-ridden activity associated with movement (Fig. 1). On visual inspection, in all infants pre-AW signals had a

<table>
<thead>
<tr>
<th>Post-menstrual age (weeks) (gestation)</th>
<th>Wt (kg)</th>
<th>Gender</th>
<th>Surgery</th>
<th>Opioid analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>39 (38)</td>
<td>2.5</td>
<td>F</td>
<td>Closure of gastroschisis</td>
<td>Morphine</td>
</tr>
<tr>
<td>43 (32)</td>
<td>3.9</td>
<td>M</td>
<td>Laparoscopic inguinal hernia repair</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>45 (40)</td>
<td>3.9</td>
<td>M</td>
<td>Laparoscopic pyloromyotomy</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>46 (40)</td>
<td>4.8</td>
<td>F</td>
<td>Excision of sacral tumour</td>
<td>Fentanyl and morphine</td>
</tr>
<tr>
<td>47 (40)</td>
<td>4.8</td>
<td>M</td>
<td>Laparoscopic pyloromyotomy</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>50 (40)</td>
<td>4</td>
<td>M</td>
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<td>Fentanyl</td>
</tr>
<tr>
<td>51 (40)</td>
<td>5.2</td>
<td>F</td>
<td>Cleft lip repair</td>
<td>Fentanyl and morphine</td>
</tr>
<tr>
<td>51 (40)</td>
<td>4.6</td>
<td>M</td>
<td>Cleft lip repair</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>51 (40)</td>
<td>6.2</td>
<td>F</td>
<td>Fashioning of rectum</td>
<td>Morphine</td>
</tr>
<tr>
<td>52 (40)</td>
<td>4.5</td>
<td>F</td>
<td>Cleft lip repair</td>
<td>Morphine</td>
</tr>
<tr>
<td>53 (38)</td>
<td>5.7</td>
<td>F</td>
<td>Cleft lip repair</td>
<td>Fentanyl</td>
</tr>
<tr>
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<td>M</td>
<td>Cleft lip repair</td>
<td>Fentanyl</td>
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<tr>
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<td>M</td>
<td>Cleft lip repair</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>63 (40)</td>
<td>7</td>
<td>M</td>
<td>Cleft palate repair</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>65 (36)</td>
<td>7.6</td>
<td>M</td>
<td>Closure of colostomy</td>
<td>Morphine</td>
</tr>
<tr>
<td>68 (40)</td>
<td>8.4</td>
<td>M</td>
<td>Closure of colostomy</td>
<td>Fentanyl and morphine</td>
</tr>
<tr>
<td>69 (40)</td>
<td>7.3</td>
<td>M</td>
<td>Cleft palate repair</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>73 (40)</td>
<td>8</td>
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<td>Renal pyeloplasty</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>77 (40)</td>
<td>7.8</td>
<td>M</td>
<td>Closure of ileostomy</td>
<td>Morphine</td>
</tr>
<tr>
<td>77 (40)</td>
<td>5.4</td>
<td>F</td>
<td>Lens capsulotomy</td>
<td>Fentanyl</td>
</tr>
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</table>
continuous low-frequency oscillation (0.5–2 Hz) with maximum amplitude varying between infants from 25 to 100 μV (median 100). In some infants in the early phase of wash-out, these low-frequency signals resembled regular transients that later merged to become continuous oscillations. In respect of frequencies ≥ 3 Hz, there were two apparent patterns related to age. The youngest infants (<52 weeks PMA) had low maximum amplitudes (median 10 μV, range 5–20), whereas older infants had higher amplitudes (median 30 μV, range 25–50). In older infants, the amplitudes of these oscillations were prominent during anaesthesia and decreased steadily during wash-out until AB (Fig. 1).

After AW, many epochs had EMG interference, and therefore, only epochs before AB have been analysed (of these only 12 epochs out of a total of 2512 were excluded). During anaesthesia, the band powers in the centro-parietal channel were approximately four times larger than those in the frontal channel. Only centro-parietal PSDs have been analysed further.

Visual analysis of power spectra showed that in almost all epochs most power was within frequencies ≤ 4 Hz and the summed power in frequencies between 20 and 70 Hz was almost always < 5 μV². During anaesthesia, however, there were two common patterns (Fig. 2). Older infants had obvious power in the range of 5–20 Hz (P5–20 Hz) (mean 308 μV², median 151 μV²).
320, range 110–542), whereas younger infants did not, and therefore, descriptive statistics were applied to these two age groups separately. In Figure 2, the power spectrum represents one infant only and shows that in that infant, the power within the 5–20 Hz band peaked at 11 or 12 Hz. This ‘peak frequency’ varied between infants and in some cases a peak frequency was not easily discerned.

The decrease in power within frequencies ≤4 Hz was often appreciable, but there were wide variations between infants so that lower 95% confidence intervals (CIs) in both age groups either included or were close to 0 (Fig. 3). For older infants, Figure 3a shows the decrease in raw power within various frequency bands. The mean reduction in power was greater in classical EEG bands than the narrow frequency bands, but the reduction in power in the P5–20 was larger than any other band (except <4 Hz) and had CIs furthest from 0 (mean decrease 252 µV², 95% CI 153–351). The mean decrease in P5–20 Hz in older infants was almost 10 times greater than that in younger infants. In the low-frequency bands (≤4 Hz), the mean and median changes in band power were dissimilar, and therefore, data were log-transformed. Figure 4 shows anti-log data in which the decrease in mean log band power is represented by the ratio between the geometric mean band powers at bSO and bAB; a ratio of 1 signifies no change in log power. For power within frequencies ≤4 Hz, 95% CIs for both young and older infants either included or were close to 1 (Fig. 4). The frequency bands 9–12, 13–16, and 8–13 Hz (alpha) had the largest

![Graph](https://academic.oup.com/bja/article-abstract/112/4/686/232193/690)

**Fig 3** Change in band power during emergence. Mean (filled circle, with 95% confidence intervals error bars) and median (open circle) decrease in band powers from anaesthesia until just before awakening in (a) infants younger and (a) infants older than 52 weeks PMA.
ratio of change in both age groups, but overall, the power reductions in the narrow and classical frequency bands were similar (Fig. 4B).

Plots showing trend over time demonstrated little change in P5–20 Hz in infants <52 weeks PMA unlike older infants in whom there was an obvious decrease (Fig. 5). Older infants had P5–20 Hz $>100 \mu V^2$ (median 320, range 110–542) during anaesthesia and by 6 min after SO P5–20 Hz had reduced to $<100 \mu V^2$ in all but two infants (Fig. 5): $P_{et}$ Sevoflurane had decreased to $<0.5\%$ in all but one infant by this time. Pearson correlation and regression coefficients for a linear model of the change in log10 P5–20 Hz over the first 5 min (50 epochs) were calculated for each infant. In older infants all except one had R-values $>0.7$ and the mean gradient was $-0.012$. This is equivalent to a decrease to 75.9 and 25.8% of the baseline by 1 and 5 min, respectively. In younger infants, the mean gradient was $-0.006$ (compared with older infants by unpaired t-test $P=0.006$).

P5–20 Hz during anaesthesia increased with age (Fig. 6); power in this frequency band of $\sim 100 \mu V^2$ separated infants younger than and those older than 52 weeks PMA. The mean frequency (in infants $>52$ weeks PMA) with the highest power in this range was 11.3 Hz (so 2.4). Age was the factor most strongly associated with P5–20 Hz. Other factors tested

![Fig 4](https://academic.oup.com/bja/article-abstract/112/4/686/232193)
were body weight, length of surgery, time taken to awaken, and
PetSevoflurane; none appreciably improved the association of
P5–20 Hz with age.

Discussion
In this small sample, the combined power in centro-parietal
EEG oscillations between 5 and 20 Hz during anaesthesia was
appreciable in infants older than 3 months of age. P5–20
decreased more than any other band power during sevoflurane
wash-out and its decrease could be a warning of inadequate
anaesthesia and impending AW.

A decrease in EEG power during sevoflurane wash-out was
also found by Davidson and colleagues5 in infants, and there
were similar EEG changes in studies in children during sevoflur-
ane anaesthesia13 and propofol sedation.13 In studies of adults
also, during induction with sevoflurane, isoflurane, or pro-
propofol,16 17 after initial low-amplitude desynchronizations, the
amplitude of oscillations in the range of 8–20 Hz increased.
Recent evidence confirms that oscillations in the alpha fre-
quency range are associated with loss of consciousness with
propofol.18 Our data show that alpha oscillations apparently
develop in infants, perhaps in a less frequency-specific form,
around the age of 3 months. In sheep, power within the
alpha range has been associated with sedation level and
benzodiazepine dose.19 In rats, AW from isoflurane anaesthe-
sia was also coincident with decrease in power of frequencies
<25 Hz, although an increase in power in higher frequencies
was a more consistent finding.20

Lo and colleagues,6 however, found that EEG power in the
8–30 Hz range increased during sevoflurane wash-out. They
maintained anaesthesia at 1.4 minimal alveolar concentration
(MAC, age adjusted), which, for sevoflurane, is ∼4% for
infants.5 At these doses, the EEG can be suppressed and
power therefore increases as anaesthesia washes out. In our
study, end-tidal sevoflurane was <2.5%, which is close to 1
MAC in infants older than 6 months21 but appreciably <1
MAC in younger infants (MAC in infant <6 months=3.2%).21

A common problem with clinical studies attempting to de-
termine the EEG effect of a steady concentration of inhaled an-
aesthetic is the variable nature of painful stimulation that
might arouse the EEG. Local anaesthesia can block stimuli
but any analgesic drugs can either directly effect the EEG or,
more likely, change the EEG indirectly by reducing the concen-
tration of vapour required to produce anaesthesia. The effect of
a fixed anaesthetic concentration can vary according to both
stimulation and other drugs. In addition, MAC might not be
constant. In a study in rats, the MAC of inhaled anaesthetics
decreased appreciably over a 4 h period in pups but not in
adults;22 23 however, the time taken to achieve equilibrium
was an important factor and was much longer than expected.
Further problems arise with the assumption that the end-tidal
concentration of sevoflurane is close to arterial. During wash-in
and wash-out phases of administration, there will be a time lag,
but even at steady-state the relationship between end-tidal
and arterial concentrations can vary.24 Our data support a rela-
tionship between EEG power and wash-out of sevoflurane, but
do not warrant an estimation of the EEG effect of a specified
sevoflurane concentration. In summary, steady-state condi-
tions are difficult to achieve and define, and might not be rele-
vant to the clinical situation when many changes are taking
place. Consequently, we have sought an EEG variable that is
robust, simple, easily computed, and potentially useful. Of all
the band powers, P5–20 Hz appears from this small data set
to be better than others. Further work is required to test its re-
liability and utility.

Total spectral power, median frequency, and SEF90 are com-
monly used descriptors of the EEG power spectrum. A problem
with these variables is that they can be dominated by high
power changes within low frequencies that can obscure the rela-
tively smaller power changes in higher frequencies. For example,
an appreciable change in total signal power might be attributable to a relatively small change in power of low frequencies that could obscure an important change in higher frequencies of low power. P5–20 Hz excludes low frequencies and therefore could be considered in isolation. Bispectral index (BIS), entropy, and other methods of processing the EEG could have been studied in this group of patients but applying additional electrodes (e.g. for BIS) would have caused practical problems, and we elected to describe the more straightforward characteristics of the EEG.

The stimulation of skin could have caused evoked changes in the EEG. In young infants, the EEG has low amplitude so that evoked potentials can have a lower signal-to-noise ratio and might be easier to identify. Evoked potentials in response to heel lancing and skin stimulation have been detected in awake preterm infants. If these are suppressed by anaesthesia their detection during emergence could prove useful in this age group.

Opioids could have both direct dose-dependent effects on EEG oscillations and indirect effects by reducing painful stimulation and EEG arousal. We think that the anaesthetists managing the infants gave sufficient opioid to prevent painful arousal although we cannot exclude a dose-related EEG effect of opioids. In 16 of our infants, we recorded EEG after induction of anaesthesia but before surgery and before opioids had been given. In comparison with the EEG recorded after surgery, EEG oscillations of frequency <5 Hz tended to have higher power before surgery and opioids, but the powers in the 5–20 Hz range were similar (geometric mean difference 1.03, 95% CI 0.3–3.7). The mean difference in end-tidal sevoflurane concentration was 0.04% (median 0.03, so 0.63, range 1.5 to 1.35). There was no obvious relationship between dose of fentanyl and time of AW. Infants who did and those who did not receive morphine awoke, on average, at the same time. There was a tendency for the youngest infants to take longest to awaken.

We found that P5–20 Hz was related to age and became appreciable at the age of 3 months. This supports data from Davidson and colleagues, who showed that band power (2–20 Hz) increases with age. At this age, there is evidence that cortical networks involving gamma-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) synaptic activity are maturing, and these may be responsible for age-related EEG changes.6

If neuronal apoptosis in the developing human brain is caused by anaesthetics, minimizing the dose would be desirable. Our data could prove useful to researchers interested in testing the efficacy of hypnotic and analgesic components of anaesthesia. In infants older than 52 weeks PMA, the cortical effects of sevoflurane during emergence could be monitored by P5–20 Hz in combination with P20Sevoflurane. If minimization of the dose of sevoflurane is intended, the dose of sevoflurane could be reduced to maintain P5–20 Hz above a set value (perhaps 100 μV²) while the absence of sympathetic arousal (increases in heart rate and arterial pressure) could be used to confirm negligible sympathetic response to stimulation. These are speculative statements and more data are required to validate our observations. In younger infants in whom the EEG during anaesthesia is ‘quiet’, research into evoked responses might be productive. If, in the future, there is concern over anaesthesia-related neurological damage, the investigation of methods of assessment of anaesthetic effect in younger infants should take priority on the assumption that infants are more vulnerable.

**Authors’ contributions**


**Acknowledgements**

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**Declaration of interest**

This work was part of a PhD (UCL) thesis (awarded to M.R.J.S. in 2010). Funding for the project was provided by a grant from the Trustees of Great Ormond Street Hospital and by the Portex Unit (part of Institute of Child Health UCL), which is supported by Smiths Medical.

- An abstract ‘The EEG during awakening from anaesthesia in infants’ was presented at Annual Scientific Meeting of the European Society of Paediatric Anaesthesiology in Warsaw on 10 September 2009.
- An abstract ‘Electroencephalographic characteristics in infants during awakening from anaesthesia’ was presented at a meeting of the Anesthesia Research Society in London on 4th December 2009. The abstract was published by the British Journal of Anaesthesia Volume 104 Issue 4 April 2010 under ‘Proceedings of the Anaesthetic Research Society Meeting’.
- An abstract of the thesis ‘Characterisation of awakening from anaesthesia in infants’ is available online at http://discovery.ucl.ac.uk/806234/.

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**References**

1 Davidson AJ. Measuring anesthesia in children using the EEG. Paediatr Anaesth 2006; 16: 374–87
Appendix

EEG epochs were not analysed if there was appreciable interference or transients\(^*\) including:

- ECG interference with amplitude greater than twice the maximum EEG amplitude.
- Transients, defined as an isolated feature, easily distinguished from background.
- K complexes, defined as single positive (upward) then negative voltage shifts of 200–300 \(\mu\)V lasting \(<1\) s.
- Sleep spindles, defined as multiple spikes of 12–14 Hz with an amplitude of 90–100 \(\mu\)V lasting 1–6 s.
- Eye-blinks, defined as steep positive change (take-off is steep but curved) with slower recovery lasting \(<1\) s.
- Accidents, defined as single acute shifts lasting \(<1\) s such as spikes (\(<200\) \(\mu\)V) and sharp waves (\(<70\) \(\mu\)V).
- EMG high-frequency ‘spiky’ signals that obscure underlying EEG.
- Non-physiological artifacts; defined as sudden steep (almost vertical take-off) changes in baseline \(>70\) \(\mu\)V lasting \(<1\) s.