British Journal of Anaesthesia Page 1 of 6
doi:10.1093/bja/aet067

BJA

Proof of concept evaluation of the electroencephalophone as a discriminator between wakefulness and general anaesthesia

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Editor's key points

- Anaesthetic monitors commonly produce an auditory output, which anaesthetists are adept at interpreting.
- The EEG waveform is complex, and changes in complex ways with changes in anaesthetic depth.
- The authors have developed a system that produces an auditory output from the transformed EEG.
- They tested the ability of anaesthetists to differentiate outputs associated with consciousness and unconsciousness.

Background. Depth of anaesthesia (DOA) monitors based on the electroencephalogram (EEG) are commonly used in anaesthetic practice. Their technology relies on mathematical analysis of the EEG waveform, generally resulting in a number which corresponds to anaesthetic depth. We have created a novel method of interpreting the EEG, which retains its underlying complexity. This method consists of turning the EEG into a sound: the electroencephalophone (EEP).

Methods. In a pilot study, we recorded awake and anaesthetized EEGs from six patients. We transformed each EEG into an audio signal using a ring buffer with a write frequency of 1 kHz and a read frequency of 48 kHz, thus elevating all output frequencies by a factor of 48. In essence, the listener hears the previous 12 s of EEG data compressed into 250 ms, updated every 250 ms. From these data, we generated a bank of 5 s audio clips, which were then used to train and test a sample of 23 anaesthetists.

Results. After training, 21 of the 23 anaesthetists were able to use the EEP to correctly identify the conscious state of $>$5 of 10 randomly selected patients ($P<0.001$). The median score was 8 out of 10, with an inter-quartile range of 7–9.

Conclusions. The EEP shows promise as a DOA monitor. However, extensive validation would be required in a variety of clinical settings before it could be accepted into mainstream clinical practice.

Keywords: consciousness monitors; electroencephalography; monitoring, intraoperative

Accepted for publication: 15 January 2013

Electroencephalographic depth of anaesthesia (DOA) monitors are commonly used in anaesthesia, but have not been conclusively shown to eliminate or even reduce the incidence of anaesthetic awareness.[1 2] There are a number of reasons why such devices might misclassify a patient's conscious state, one of which is the electronic algorithm used to process the raw electroencephalogram (EEG) into a number intended to correlate with anaesthetic depth.[3] Research efforts have focused on refining such algorithms or inventing new ones, but the reality is that no major conceptual advance in the technology of EEG-based DOA monitors has occurred in over a decade. Here, we outline a novel method of interpreting the single channel spontaneous frontal surface EEG, which shows promise in functioning as a DOA monitor: the electroencephalophone (EEP). Outputting the electroencephalographic waveform as a sound bypasses the need for complex mathematical manipulation of the EEG, since the human ear is uniquely suited to processing intricate analogue signals in raw form.[4]

The primary aim of the study was to assess the feasibility of transforming the spontaneous EEG into a sound. Secondary aims were to optimize the sound for detecting that an anaesthetic has been administered, and to prove the concept that the EEP can function as a DOA monitor, by testing the null hypothesis that a subject using the EEP would perform no better than random chance in determining the conscious state of a given patient.

Methods

Ethics approval and patient population

We obtained approval for the study from the West of Scotland Research Ethics Committee (REC no. GN11AN376; R&D

no. 11/WS/0101). Written informed consent was obtained from each patient.

Six adult patients, undergoing elective orthopaedic surgery, without paralysis, of ASA grade I–II, were enrolled in this pilot study. Exclusion criteria were previous neurological diagnosis (e.g. epilepsy), or surgery where access to the forehead was limited by positioning or drapes (e.g. prone or deckchair positions).

After data collection and transformation into the EEP, 23 anaesthetists took part in an online module where they listened to the audio recordings. The ethics committee waived the requirement for written consent for this activity.

Study protocol

After cleaning with an alcohol wipe, three standard electrocardiogram (ECG) electrodes were attached to each patient. The positive electrode was attached to the forehead (Fp2), the negative electrode to the right zygoma and the ground electrode to the left zygoma. The electrodes were attached by short cables to a preamplifier and data acquisition (DAQ) board (USB-DUX-sigma, Incite Technology Ltd, Stirling, UK) which fed into a laptop computer. The DAQ board also provided electrical isolation of the patient. A real-time display of EEG confirmed an adequate electrode placement. The patients did not receive premedication. Before administering anaesthesia, patients were asked to lie still for 5 min so that a baseline reading could be obtained. Anaesthesia was induced with propofol titrated to effect, and fentanyl 1.5 mg kg^{-1}. The airway was maintained with a laryngeal mask airway, and anaesthesia was maintained with sevoflurane 1.5–2 in 50% oxygen with spontaneous ventilation in a circle system. Further opiates were administered at the discretion of the attending anaesthetist.

Event marking on the laptop computer was used for the baseline period, at induction of anaesthesia, whenever a disturbance resulted in artifact, and at the point where end-tidal sevoflurane consistently read 80% of predicted MAC for age. Five minutes after this point, recording was discontinued. The clinical and MAC-guided determination of adequate anaesthesia was subsequently supported by off-line analysis of the EEG using the relative beta ratio (BetaRatio), an EEG parameter which has been previously validated.[5–7]

EEG signal processing

We amplified the EEG with a standard two stage instrumentation amplifier: first by a factor of 10, then the direct current filtered signal by a factor of 50, which gave an overall gain of 500. The signal was then digitized with a sampling rate of 1 kHz and resolution of 24 bits (Fig. 1). To avoid aliasing the signal was low-pass filtered. After digitization, the 50 Hz mains signal was removed, frequencies <10 and >200 Hz were eliminated, and automatic gain control employed so that the output from all samples would have the same audio volume. The central difficulty in making the EEG audible is that its frequency range is too low for the human ear. After some experimentation, we decided to play the EEG faster and at the same time repeat it cyclically. This was done by means of a ring buffer. The EEG was written to the buffer at a rate of 1 kHz, but read from the buffer at a rate of 48 kHz, thus multiplying all frequencies in the EEG by 48. The buffer size was 12 000 ms and was read every 250 ms meaning that, in essence, the listener hears the

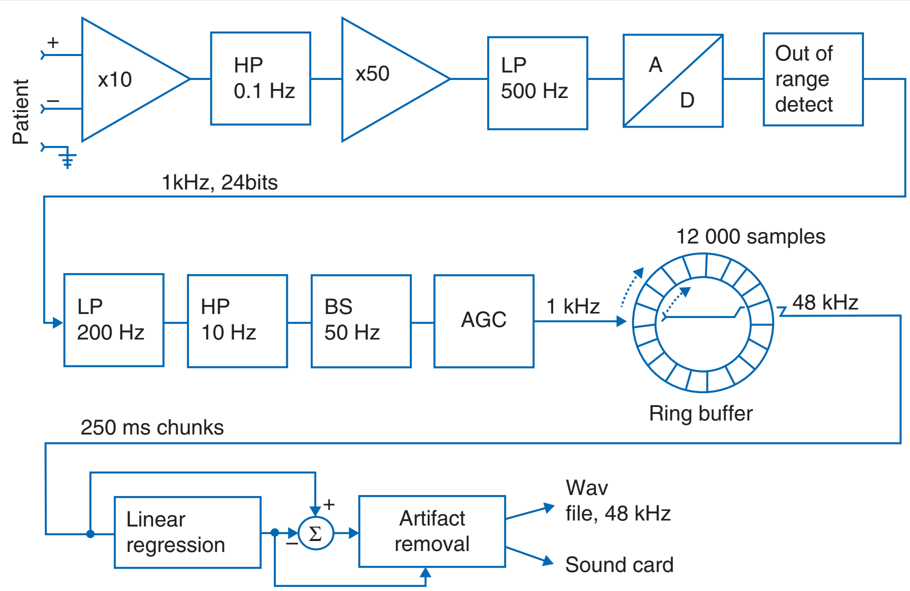

Fig 1 Schematic flow diagram to show generation of EEP from raw EEG. HP, high-pass filter; LP, low-pass filter; A/D, analogue-to-digital converter; BS, band-stop filter; AGC, automatic gain control.

previous 12 s of EEG data compressed into 250 ms, updated every 250 ms.

Because the output consists of discrete epochs of 250 ms, discontinuities exist when they are concatenated into a continuous stream. To have a more seamless transition between epochs, we performed a linear regression on each one and subtracted the result from the EEG data for that epoch. This process also removed any residual direct current from the signal (which should not be present in audio output).

The regression coefficient was then used to reject gross artifact: if the slope of the signal for an epoch was higher than a threshold (0.0001) then the presence of artifact was assumed and the previous epoch was repeated instead. In practice, this happened ~5% of the time.

The final audio signal at a sampling rate of 48 kHz was sent to a sound card.

All computer processing was written in C, with the facility for real-time processing of both EEP and BetaRatio.

EEP evaluation

After transformation into the EEP, a bank of 5 s audio clips was created, along with an online testing module (http://www.berndporr.me.uk/eepquiz/). This module was accessed remotely (after email invitation) by 23 anaesthetists, to determine whether they could learn to use the EEP to recognize a patient's conscious state. The bank of audio clips used in the module (66 in total) was drawn randomly from periods when patients were awake and lying still ('awake'), and from periods after the MAC value reached 80% and BetaRatio was <-1 ('anaesthetized'). The 20 clips used for training were chosen from the complete bank by the researchers. The 10 clips used for the final test were chosen by computer, at random, from the remaining 46. First, 10 training samples were played where the subjects were told in advance what they were about to hear. Awake and anaesthetized samples alternated. Then, 10 new training samples were played in random order and the subjects asked to decide whether the patient was awake or anaesthetized. At the end of each sample, the subjects were told whether they were right or wrong. Finally, the subjects were tested on 10 further samples, presented by the computer in random order, without any answers being given. Answers from this test were automatically recorded to a database.

To formally test the null hypothesis that subjects using the EEP would perform no better than random chance, we used the binomial test. If the EEP is no better than chance, then approximately half the subjects should score between 1 and 5 out of 10, and half should score between 6 and 10 out of 10. The test is thus executed by entering the number of subjects who score ≥ 6 into a two-tailed binomial calculation, with a baseline probability of 0.5. To perform the binomial calculation we used the open source statistical/mathematics package R.

Results

It was possible to record sufficient EEG data for processing in all six patients. An example of frequency spectra obtained from an awake and an anaesthetized patient is shown in Figure 2. Transformation of the EEG to the EEP is described above. Twenty-three anaesthetists completed the online testing module, and a histogram depicting their performance is shown in Figure 3. The contingency table for all responses in the online test is given in Table 1. The median score for the test was 8 out of 10, with an inter-quartile range of 7–9. Twenty-one of the 23 anaesthetists were able to correctly identify the conscious state of >5 of 10 patients. The probability of this happening when the null hypothesis is true is <0.001.

Discussion

Main findings

In this study, we have demonstrated that it is possible to generate a sound from the spontaneous single channel surface EEG, which can differentiate between the awake

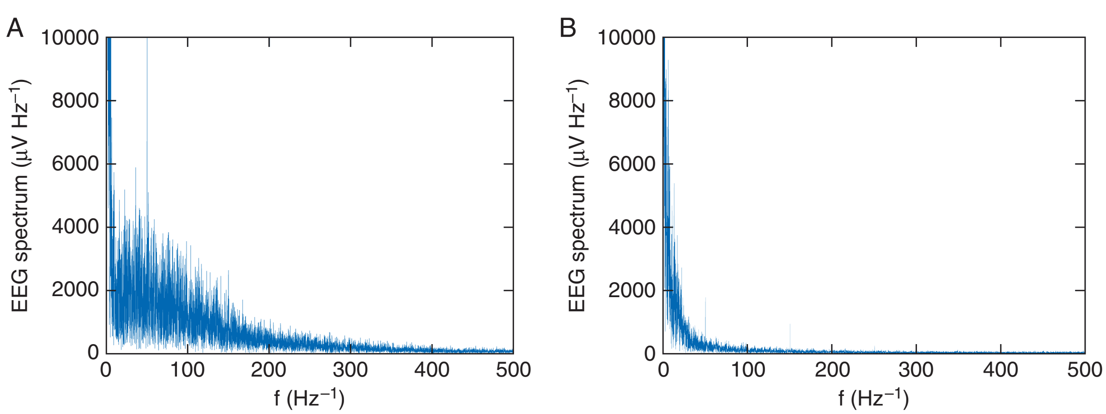

Fig 2 Example of amplitude spectra from a representative 20 s sample obtained from an awake (A) and an anaesthetized (B) patient.

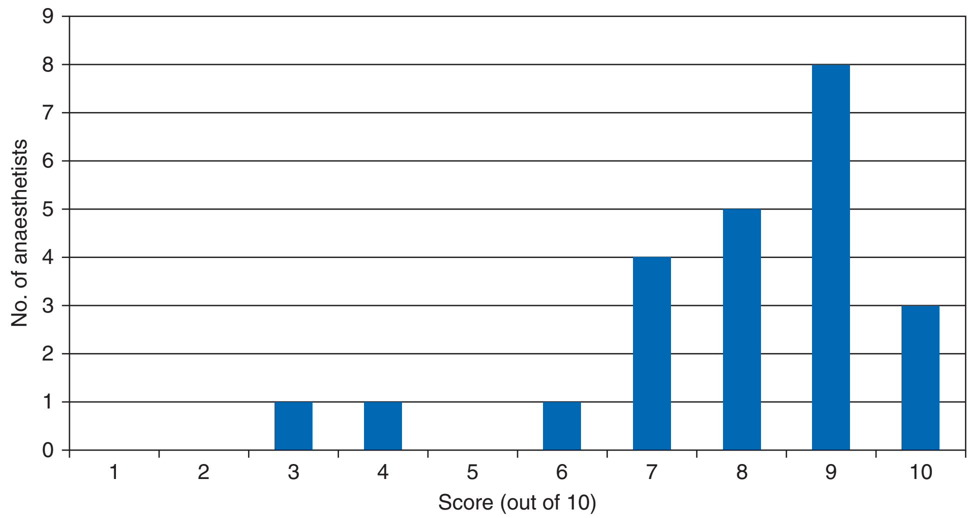

Fig 3 Histogram of anaesthetists' performance in EEP test (n=23).

Table 1 Contingency table of all submitted responses to EEP online test (23 subjects submitted 10 responses each)

	Actually awake (n=110)	Actually anaesthetized (n=120)	Total
Answer awake	89	26	115
Answer anaesthetized	21	94	115
Total	110	120	230

and anaesthetized state. With <2 min of training, most anaesthetists could categorize the conscious state of our sample of patients, from 5 s of exposure to their raw EEG data.

Previous studies

While there are no previous studies using this technique, the concept of the EEP is not new. A primitive version was in fact patented in 1971 for the purpose of facilitating meditation.[8] Likewise, the use of raw audio signals within otherwise complex systems is not unheard of, for example, the hydrophone on a submarine. However, the use of the EEP in the context of mainstream medicine or anaesthesia appears to be novel.

Differences from previous EEG monitoring studies

Our methodology was designed to be as simple as possible, and we used non-proprietary hardware and software. We used ECG electrodes, which have previously been shown to be non-inferior to specialized EEG electrodes, and are readily available.[9] We used a freely available algorithm (the BetaRatio) for the quantification of anaesthetic depth, which has been validated against the BIS monitor® (of which it is a component) and other electroencephalographic indices.[5 6 10] Our EEG-acquisition module was a generic high-sensitivity instrumentation amplifier of low cost.

In terms of generating the EEP itself, there was no relevant previous work to emulate. We decided to use the simplest software transformation available, the ring buffer.[11] This enabled preservation of EEG morphology. Upscaling the EEG by a factor of 48 allowed us to utilize the sensitivity curve of the ear, by mapping the higher frequencies of the EEG to the part of the auditory spectrum (2000–5000 Hz) where the ear is most sensitive.[12] This avoided the need for the preprocessing seen in some computerized DOA monitors, where differentiation of the EEG is used to emphasize high frequencies at the expense of adding substantial noise.[5 13] We chose a repetition frequency of 4 Hz because it offered a balance between two problems: the obliteration of the audio signal by hum seen with a high repetition frequency, and the potential for trapping of artifact in the buffer with a low repetition frequency.

We included EEG frequencies up to 200 Hz to include the gamma frequency band, a component of the EEG which has previously been reported to correlate with memory formation and with the conscious state.[14 15] Standard monitors only include frequencies up to 47 Hz.[5] However, this limitation risks omitting pertinent information relating to conscious state (see http://www.berndporr.me.uk/eep_supp/ for a comparison).

Our artifact removal process was simple, and directed at only gross, high amplitude artifact. This is in contrast to computerized DOA monitors, whose complex artifact handling algorithms may actually contribute to misclassification of patient state.[16] It is feasible that a sufficiently trained listener will learn to identify sounds generated by typical artifactual contaminants such as diathermy.[17]

Strengths and weaknesses in EEP/study

The EEP has several potential advantages over existing systems. First, it presents EEG data in real-time, unlike computerized monitors where Fourier transformation introduces an inevitable lag. The BIS monitor®, for example, has a lag time of over a minute, during which significant clinical change could have occurred unnoticed.[17 18] Secondly, the EEP need not be a standalone system, but could be used in tandem with processed EEG parameters. The BetaRatio may be particularly useful for this purpose as it can also be computed and presented in real-time, thus eliminating one of the largest barriers to effective DOA monitoring. Thirdly, a listener using the EEP will have access to paired data, because he will have heard the same patient in both the awake and the anaesthetized state. Finally, the device would offer a constant audio presence capable of alerting the clinician to a change in patient state, even if his attention is elsewhere.

This pilot study clearly has limitations. First, we only recorded EEGs from six patients. Secondly, like all DOA monitors, the contribution of the electromyogram to the signal is difficult to quantify without paralysing awake volunteers.[19 20] Thirdly, several of our technical decisions on how to generate the EEP were, of necessity, arbitrary and could be challenged. Fourthly, our results, while statistically significant, are not clinically sufficient to warrant adoption of the EEP as a DOA monitor in its current iteration. Fifthly, we looked only at the dichotomous outcome of awake *vs* anaesthetized.

The very concept of the EEP also has flaws. First, the limitations of EEG-based monitoring apply perforce to the EEP. This includes the fact that it is a phenomenological signal, lacking a robust neurobiological theoretical basis. Secondly, many would feel that additional noise in the operating theatre is undesirable, although this could be overcome by the use of an earpiece. Finally, some anaesthetists would doubtless prove to have a cloth ear and would find the device useless.

Future studies

If this technique is felt to have potential, then extensive validation would be needed in a variety of settings. Confirmation of feasibility would require use of the isolated forearm technique during emergence from anaesthesia. Clinicians would have to undergo training in use of the EEP, which in turn would necessitate the creation of an EEP library. It would also have to be determined whether it is possible to assess gradations of anaesthesia (including burst suppression) using the technique.

Conclusion

The existence of a national audit project looking at unintended awareness under anaesthesia is a reminder that the currently available methods of assessing anaesthetic depth are not perfect. Efforts to reduce the incidence of awareness will clearly be multifactorial, but an important part of the work remains the search for a more reliable DOA monitor.

The EEP represents a significant conceptual departure from the current paradigm of mathematically-derived DOA indices. It avoids the need for complex mathematical transformations, and uses open source technology. It differentiates well between the awake and anaesthetized states, and can be used with minimal training. We believe that it merits further evaluation.

Acknowledgements

We thank Dr Tom Aitchison and Professor Alistair Chalmers for their statistical advice. J.G. thanks Dr Martin Bartos for rediscovering the term ‘electroencephalophone’.

Declaration of interest

B.P. is co-owner of Incite Technology Ltd.

Funding

This work was supported by internal funds from NHS Greater Glasgow and Clyde, and the University of Glasgow.

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Handling editor: A. R. Absalom