Postoperative changes in visual evoked potentials and cognitive function tests following sevoflurane anaesthesia

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We tested the hypothesis that minor disturbance of the visual pathway persists following general anaesthesia even when clinical discharge criteria are met. To test this, we measured visual evoked potentials (VEPs) in 13 ASA I or II patients who did not receive any pre-anaesthetic medication and underwent sevoflurane anaesthesia. VEPs were recorded on four occasions, before anaesthesia and at 30, 60, and 90 min after emergence from anaesthesia. Patients completed visual analogue scales (VAS) for sedation and anxiety, a Trieger Dot Test (TDT) and a Digit Symbol Substitution Test (DSST) immediately before each VEP recording. These results were compared using Student's t-test. P<0.05 was considered significant. VEP latency was prolonged (P<0.001) and amplitude diminished (P<0.05) at 30, 60, and 90 min after emergence from anaesthesia, when VAS scores for sedation and anxiety, TDT, and DSST had returned to pre-anaesthetic levels.

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In 1997, 60% of all elective surgical procedures in the USA were done on a ‘day case’ or ambulatory basis.1 In these patients, rapid, complete recovery from the effects of anaesthetic agents is desirable. Clinical, psychomotor, and cognitive tests can measure recovery from the residual effects of anaesthetic agents.2 3 Although cognitive and psychomotor tests are normal by the second day after operation, subjective cognitive impairment can persist for 3 days.4 Patients who have been discharged probably have minor degrees of residual anaesthetic effect, with implications on safety as patients resume normal activities of daily living.

The effect of anaesthetic agents on visual evoked potentials (VEPs) has not been studied in the postoperative period. Minor degrees of disturbance of the visual pathway could persist following general anaesthesia.

Of the evoked potentials in clinical use, VEP is the most sensitive and brainstem auditory evoked potentials are the most resistant to drug effects.5 6 Because hearing is the last sensory modality to be abolished and the first to return at light levels of anaesthesia, the effects of anaesthesia on the auditory evoked potentials are well known, in relation to monitoring depth of anaesthesia.7 VEPs have been studied mostly in the context of testing the integrity of the visual pathway during surgery near the optic chiasm.7 Anaesthetic agents (both volatile and i.v.) affect the latency and amplitude of VEP.5 6 8–10 16–19

We conducted a prospective observational study (1) to quantify the effect of sevoflurane anaesthesia on VEP amplitude and latency in the early (90 min) postoperative period and (2) to examine the association between VEP changes and standard tests of cognitive and psychomotor function.

Methods

With institutional ethical approval, and having obtained written informed consent, we studied 13 ASA I or II patients about to have non-neurological, elective surgery. Patients with decreased visual acuity or hypo- or hyperthermia were excluded from the study.

No pre-anaesthetic medication was administered. VEPs were recorded on four occasions; on arrival to the anaesthetic room preoperatively and at 30, 60, and 90 min after the operation using a portable four-channel evoked potential monitoring system (Neuropack 4 mini MEB5304K, Nihon
Three transcutaneous ‘active’ electrodes were placed on the occiput and an ‘indifferent’ or reference electrode on the midfrontal region. The electrode impedance accepted at the time of measurement was <5 kOhm. Standard EEG disc electrodes were stuck on the scalp by means of a water soluble conducting EEG paste (Ten 20™, D.O. Weaver and Co., USA) and secured in place using a ‘swim cap’. A domestic television set placed at a distance of 1 m was used to generate a pattern reversal stimulus of constant luminance, consisting of black and white checks, which alternate abruptly. Moderate room illumination was used during testing. Pattern stimuli were presented at 2 Hz and 100 measurements amplified and digitally averaged to produce the VEP with automatic estimation of latency and amplitude via an Apple Macintosh computer software (Framefile reporting V2.4). However a neurophysiology technician unaware of the time of the recording (relative to anaesthesia) selected the point of maximal response.

A Trieger Dot Test (TDT) and a Digit Symbol Substitution Test (DSST) were carried out before the operation and immediately before the VEP recordings at 30, 60, and 90 min after the operation. The TDT is a measure of psychomotor function. The subject is presented with a figure composed of 41 dots and asked to connect them by a pencil mark in 40 s or less. A score is assigned according to the number of dots omitted. The DSST is a measure of cognitive function and it has been shown to be sensitive even to small degrees of sedation. To do the test, the subject is asked to integrate visual scanning speed with number substitution for 110 given symbols. The test is scored according to the number of correct entries obtained in 90 s. This test is a sensitive measure for residual cortical dysfunction.

Subjective assessments were made with standardized visual analogue scales (VAS) for sedation and anxiety at each timepoint. The VAS consisted of two 100-mm lines, such that 0=minimal impairment and 100=maximal impairment, representing drowsiness (0=fully awake and alert, 100=extremely drowsy) and anxiety (0=calm and 100=excited).

With standard monitoring in place (pulse oximetry, electrocardiography, non-invasive arterial pressure, and inspired and end tidal partial pressures of sevoflurane, nitrous oxide and oxygen (Datex AS/3 monitor, Datex Corp., Helsinki, Finland) anaesthesia was induced with 8% sevoflurane in 100% oxygen. General anaesthesia was maintained by inhalation of clinically indicated concentration of sevoflurane in a 53% oxygen/66% nitrous oxide mixture. Temperature was monitored by a naso- or oropharyngeal thermistor (YSI 400 Series, Mallinckrodt Medical, Inc., St Louis, USA). Intraoperative analgesia was fentanyl (1–1.5 µg kg⁻¹), diclofenac 100 mg p.r., or tenoxicam 20 mg i.v. and a local/regional block with 0.5% bupivacaine. Intermittent positive pressure ventilation was used to maintain $P\text{ET}_{CO_2}$ between 4.0 and 4.5 kPa. Muscle relaxation, when indicated, was with 0.1 mg kg⁻¹ vecuronium and incremental doses as necessary, monitored using a transcutaneous nerve stimulator (MiniStim MS-
III A, Life-Tech, Inc., Houston, USA) and antagonized with neostigmine 50 μg kg⁻¹ combined with 10 μg kg⁻¹ glycopyrrolate. End-tidal sevoflurane (FE₉₅₉) concentrations were recorded immediately before tracheal extubation or removal of laryngeal mask airway (LMA).² On arrival in the postoperative recovery area a post-anaesthesia recovery score of Aldrete and Kroulik₁⁶ was noted (Table 1).

Cognitive (DSST) and psychomotor (TDT) tests, VAS, and VEP measurements were expressed in terms of mean (SD) and compared using Student’s t-test. P < 0.05 was considered significant. Correlation was sought between change in VEP amplitude and latency and anaesthetic time, using Pearson’s correlation coefficient.

Results
Thirteen (three male and 10 female) ASA I and II patients aged 41 (15, range 19–62) yr were studied. Data obtained from the first patient were not included in the analysis because of inadequate quality of VEP recording caused by large electrode impedance. Seven patients underwent excision of breast lump, three had hysteroscopy, and another three underwent removal of screw/plate from a limb. Anaesthesia and analgesia were not standardized. All patients were given fentanyl 1.5 μg kg⁻¹, followed by local infiltration or limb block (one brachial plexus and two combined femoral and sciatic nerve blocks) with 0.5%

Fig 1 Characteristic VEP recordings from stimulation of the left eye of a patient obtained before (top) and at 30, 60, and 90 min after anaesthesia (bottom). A1-3 represents the recordings from the active electrodes. The cursor indicates the time of maximal evoked response (latency).

Fig 2 Sedation and anxiety measurements. T₀ represents the time before anaesthesia (baseline). T₁, T₂, and T₃ represent 30, 60, and 90 min after emergence from anaesthesia, respectively. *P < 0.001 compared with pre-anaesthetic values, †P = 0.01 compared with pre-anaesthetic scores.

²LMA is the property of Intavent Limited.
bupivacaine. Eight patients had diclofenac 100 mg p.r. and five had tenoxicam 20 mg i.v. One patient required a neuromuscular blocking agent (vecuronium 0.1 mg kg⁻¹). Body temperatures were normal.

Duration of anaesthesia was 57 (sd 21) min and end-tidal sevoflurane concentration before tracheal extubation or removal of LMA was 0.23 (0.05). Aldrete scores on arrival in recovery were 10 in two cases and 9 in the remaining 10 cases (Table 2). Characteristic VEP recordings after stimulation of the left eye of a patient at the four times are shown in Figure 1. The latency increased from 109 ms to 129, 120 and 114 ms at 30, 60, and 90 min after the operation, respectively. The amplitude decreased from 15 to 12 μV at 30 and 60 min and returned to 15 μV at 90 min.

Figure 2 shows the VAS for sedation and anxiety. Patients felt more drowsy at 30 (P=0.001) and 60 min (P=0.010) after emergence from anaesthesia than before anaesthesia. The VAS scores for sedation at 90 min after anaesthesia and the preoperative baseline were not significantly different (P=0.315). Pre- and post-anaesthetic anxiety scores were similar.

TDT scores were greater at 30 min (P=0.001) after emergence from anaesthesia, but there was no difference at 60 (P=0.181) and 90 min (P=0.251) compared with the pre-anaesthetic scores (Fig. 3). DSST scores decreased at 30 min (P<0.001), were similar to the pre-anaesthetic scores at 60 min (P=0.39) and increased at 90 min (P=0.020), presumably because of learning (Fig. 3).

The latency of VEP was prolonged at 30 (P<0.001 on both sides), 60, and 90 min (P<0.05 on the right and P<0.001 on the left) after emergence from anaesthesia compared with the pre-anaesthetic values, as shown in Figure 4. The amplitude of VEP was reduced on both sides at 30 (P<0.01) and 60 min (P<0.01) after emergence from anaesthesia, and this was maintained at 90 min on the right side (P=0.016). There was no correlation between the duration of anaesthesia time and changes in VEP latency or amplitude.

**Discussion**

We found that VEP latency is prolonged 90 min after sevoflurane anaesthesia, when measures of psychomotor and cognitive function and sedation have returned to normal. Thus VEP latency may indicate postoperative residual anaesthetic effect.

Previous studies have shown a dose-related effect of inhalational agents (halothane, enflurane, and isoflurane) on VEP latency and amplitude. Nitrous oxide causes a dose-related decrease in VEP amplitude but not latency. Similarly, these findings apply to VEP recorded during anaesthesia, whereas our first VEP measurement was performed 30 min after discontinuation of nitrous oxide administration. Neither fentanyl nor neuromuscular blocking agents influence VEP latency or amplitude. Loughnan and colleagues showed that i.v. fentanyl 200 μg has no effect on evoked potentials. The maximum dose of fentanyl used in our study was 120 μg, so it is likely that the changes in VEP latency and amplitude in this study are related to sevoflurane administration.

Using ‘within patient’ comparisons, and anaesthesia with a single agent, sevoflurane, known to influence VEP,
reduced possible confounding variables. Temperature and systemic arterial pressure can influence VEP, but these were normal in all patients throughout the study. To reduce variation in technique, all VEP recordings were carried out by a single investigator. Latency and amplitude measurement points were then selected by a second investigator who did not know when the recordings had been obtained.

One limitation of this study is that the ‘learning effect’ for the TDT or DSST was not quantified. The improvement in DSST scores at 90 min suggests that some learning effect was present. The psychometric tests show that no gross deficit in cognitive or psychomotor function is present at the time of prolonged VEP latency.

Although a relatively small number of patients (13) was studied, VEP changes were consistent and varied little between patients.

The changes in VEP latency and amplitude were not related to the duration of anaesthesia. However, duration of anaesthesia is a poor indicator of cerebral anaesthetic partial pressure, especially following discontinuation of volatile anaesthesia is a poor indicator of cerebral anaesthetic partial pressure in the residual effects of the agent (washout). It is very likely that the effects on VEP latency and/or amplitude persist after current discharge criteria from recovery room are met.

In conclusion, we found that VEP measurement, a non-invasive, reproducible bedside technique, indicates a residual effect of sevoflurane. In view of previous studies on intraoperative VEP, this effect is likely to be true for other inhalation anaesthetic agents, especially when considering the low blood:gas partition coefficient (0.63–0.69) of sevoflurane. The low solubility of sevoflurane in blood suggests that alveolar:inspired concentrations should decrease rapidly upon cessation of the agent (washout). It is very likely that the effects on VEP latency and/or amplitude persist after current discharge criteria from recovery room are met.

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