Anaesthesia for magnetoencephalography in children with intractable seizures

PETER SZMUK MD*,‡, SPENCER KEE MD*, EVAN G. PIVALIZZA MBChB, FFASA*, ROBERT D. WARTERS MD*, DAVID C. ABRAMSON MD, MBChB, FAAP* AND TIBERIU EZRI MD†‡

*Department of Anesthesiology, University of Texas Medical School at Houston, Houston, TX, USA, †Department of Anesthesia, Wolfson Medical Center, Holon, affiliated to Sackler School of Medicine, Tel Aviv, Israel and ‡Outcomes Research™ Institute, Louisville, KY, USA

Summary

Background: Magnetoencephalography (MEG), a noninvasive technique for evaluation of epileptic patients, records magnetic fields during neuronal electrical activity within the brain. Anaesthesia experience for MEG has not yet been reported.

Methods: We retrospectively reviewed records of 48 paediatric patients undergoing MEG under anaesthesia. Thirty-one patients (nonprotocol group) were managed according to the anaesthesiologist’s discretion. Premedication included oral midazolam, chloral hydrate or fentanyl oralet, intravenous midazolam or inhalational anaesthesia with sevoflurane. Anaesthesia was maintained with propofol, midazolam, fentanyl, alone or in combination. A subsequent protocol group (17 patients) received chloral hydrate as premedication and propofol for maintenance of anaesthesia.

Results: There was an overall 25% failure of interictal activity and localization on the MEG scan. In the nonprotocol group, 11 scans failed (35.5%). Of these, eight (72.7%) received midazolam orally. Only one failure (5.8%) was recorded in the protocol group in a patient who received chloral hydrate as sedation supplemented by sevoflurane.

Conclusions: In our experience, midazolam premedication resulted in a high MEG failure rate (73%). Chloral hydrate premedication and propofol maintenance resulted in a lower incidence of MEG failure (5.8%). General anaesthesia with a continuous infusion of propofol or sevoflurane appears acceptable, although, lighter levels of anaesthesia might be required to avoid interference with interictal activity of the brain.

Keywords: magnetoencephalography; epilepsy; seizures anaesthesia
**Introduction**

Magnetoencephalography (MEG) is a noninvasive technique for the evaluation of epileptic patients with complex intractable seizure disorders that records the magnetic fields induced during neuronal electrical activity within the brain (1–3). When information from the MEG is coupled with a magnetic resonance image (MRI) of the brain, the resultant magnetic source image provides stereotactic information for potential surgical excision of epileptic foci (4,5).

The majority of patients undergoing MEG are cooperative adults who do not require anaesthesia. However, children with complex seizure disorders and behavioural problems cannot remain quiescent for the study. The MEG is conducted in a magnetically shielded room (MSR) necessitating location of monitoring equipment outside. Limited access to the patient’s airway, poor lighting, remote location, and the need for adequate monitoring and emergency equipment all present challenges within the MEG environment. Premedication with an antiepileptic agent, barbiturate or benzodiazepine causing suppression of electrical cortical activity might lead to MEG failure while the use of epileptogenic drugs may precipitate seizures in a remote location where the airway management may be difficult from a logistic point of view.

To date, anaesthesia experience for MEG has not been described. We present our experience with 48 paediatric patients who underwent MEG scans at our institution.

**Methods**

This was a retrospective study, with approval by the Committee for the Protection of Human Subjects at the University of Texas at Houston; evaluating anaesthesia provision for children undergoing MEG scans. Data were collected on all MEG scans requiring anaesthesia from January 1998 to November 2001. Scan data were collected from computerized records registered in the MEG department database, and anaesthesia data were collected from the hand-written anaesthesia records.

The MEG suite consists of a MSR and a command room. The anaesthesia equipment is located in the command room, just outside the MSR necessitating long monitor cords and intravenous (IV) tubing to reach the patient. In cases, where general anaesthesia with a tracheal tube was used, the anaesthesia machine was placed in the MSR.

Monitoring consisted of ECG, noninvasive blood pressure, pulse oximetry, and capnography during general anaesthesia with tracheal intubation.

Following sedation, IV access was secured in the day surgery unit or the command room adjacent to the anaesthesia machine if use of inhalational anaesthesia was anticipated. The patient was moved into the MSR and electroencephalogram (EEG) and other electrodes (e.g. for somatosensory mapping) were applied. The MEG helmet, containing the helium filled magnetic sensors was applied to the patient’s head.

The patient was left alone in the MSR, although an observer was permitted to stay inside if he/she kept absolutely still. Visual contact with the patient was maintained continuously through a closed circuit television monitor located in the command room. In case of emergency, the patient could be reached in less than 10 s. In cases requiring airway assistance, the anaesthesia machine was placed just into the MSR to facilitate airway control.

Between January 1998 and February 2000, patients were premedicated as necessary, according to the anaesthesiologist’s discretion. This initial nonprotocol group of patients was designated as study group 1. After analysing the initial failure rate, a subsequent protocol group (group 2) (from February 2000 to November 2001) of patients were managed by sedation with chloral hydrate and if necessary, with N₂O/O₂ and sevoflurane only for IV cannulation. Thereafter, propofol was used, if required, as intermittent bolus or as a continuous infusion. The anaesthetic drugs used and their doses are presented in Table 1.

Patient demographics, anaesthetic management, and MEG scan failures are expressed as mean ± sd or as absolute number of cases and percentage of the total. Data analysis was performed with the Student’s t-test for continuous parameters or the chi-square test for noncontinuous parameters.

**Results**

Demographical data and the duration of anaesthesia for MEG alone and together with MRI are presented
Table 1
Anaesthetic management

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 31)</th>
<th>Group 2 (n = 17)</th>
<th></th>
<th>Group 1 (n = 31)</th>
<th>Group 2 (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>7 (22.5%)</td>
<td>–</td>
<td>1 (3.2%)</td>
<td>3 (17.6%)</td>
<td></td>
</tr>
<tr>
<td>Midazolam PO (0.5–1 mg·kg(^{-1}))</td>
<td>8 (25.8%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Midazolam IV (0.05 mg·kg(^{-1}))</td>
<td>1 (3.2%)</td>
<td>–</td>
<td>2 (6.4%)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Chloral hydrate (50–100 mg·kg(^{-1}))</td>
<td>9 (29%)</td>
<td>17 (100%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Clonidine 5 µg·kg(^{-1})</td>
<td>4 (12.9%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fentanyl orate (15 µg·kg(^{-1}))</td>
<td>1 (3.2%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fentanyl IV (1 µg·kg(^{-1}))</td>
<td>1 (3.2%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>6 (19.3%)</td>
<td>4 (23.5%)</td>
<td>6 (19.3%)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Propofol*</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>No of patients (%)</td>
<td>25 (80.6%)</td>
<td>14 (82.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total dose (mg·kg(^{-1}))</td>
<td>88.7 ± 47</td>
<td>98.4 ± 57</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PO, per os; IV, intravenous.

Group 1, nonprotocol group; group 2, protocol group.

*Propofol was administered as bolus 2 mg·kg\(^{-1}\) to facilitate intubation in six patients receiving sevoflurane induction or as bolus 0.2-0.3 mg·kg\(^{-1}\) during maintenance of anaesthesia or in continuous infusion 50-100 µg·kg\(^{-1}\) min\(^{-1}\).

Table 2
Demographic characteristics of patients and duration of anaesthesia

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 31)</th>
<th>Group 2 (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>5.7 ± 4.3</td>
<td>4.9 ± 2.3</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>30 ± 12</td>
<td>27 ± 11</td>
</tr>
<tr>
<td>MEG duration (min)</td>
<td>88 ± 51</td>
<td>95 ± 64</td>
</tr>
<tr>
<td>Total anaesthesia duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEG + MRI</td>
<td>260 ± 90</td>
<td>278 ± 106</td>
</tr>
<tr>
<td>(n = 33)</td>
<td>(n = 21)</td>
<td>(n = 12)</td>
</tr>
</tbody>
</table>

MEG, magnetoencephalography; MRI, magnetic resonance imaging.

Group 1, nonprotocol group; group 2, protocol group.

There were no significant differences between the two groups with regard to total propofol dose (88.7 ± 47 mg·kg\(^{-1}\) in group 1 vs 98.4 ± 57 mg·kg\(^{-1}\) in group 2). Sevoflurane was used for maintenance in 19% of the cases in group 1.

Interictal activity and localization were achieved in 36 (75%) of all cases. Localization failure was caused by overpowering delta waves (four cases = 7%), beta waves (four cases = 7%), lack of spikes (three cases = 7%) and inability to localize despite interictal MEG activity (one case = 3.5%). In group 1, 11 of the 31 scans failed (35.5%), compared with a single failure (5.8%) of 17 patients in the protocol group (Table 3) (P < 0.001). Of the 11 failed cases in group 1, eight (73%) received midazolam premedication. In seven of these, anaesthesia was maintained with propofol infusion and one patient was maintained with N\(_2\)O/O\(_2\)/sevoflurane. Of the remaining three failed cases, two (18%) were anaesthetized and maintained with sevoflurane and one (9%) received chloral hydrate as premedication. This patient received propofol and midazolam for maintenance. The only patient with failed interictal activity in the protocol group had chloral hydrate as sedation supplemented by sevoflurane during the IV line placement. Anaesthesia was maintained with propofol. Only one patient receiving midazolam per os (PO) had a successful scan.

When somatosensory mapping was attempted (50% of cases), there was a 29.1% (seven cases) failure rate. Two patients received propofol anaesthesia,
three midazolam premedication with propofol maintenance, and two received midazolam premedication with no anaesthetic maintenance.

One child (8 years) developed grand mal seizures 1.5 h after start of the MEG scan following chloral hydrate premedication. Convulsions were managed with two boluses of 1 mg each of intravenous midazolam, with no further complications and the MEG scan was discontinued.

Discussion

The MEG helps localize epileptic foci in the brain of patients suffering from convulsions both in adults and children (6–8). Magnetic fields generated in the brain are very tiny: of the order of $10^{-15}$ Tesla. The Earth has a uniform magnetic field, which is about $10^{10}$ power greater than cerebral magnetic fields. Urban noise from power lines, transformers, electrical appliances, and cars generate a changing loud source of interference. This clutter is screened out by placing the patient into a specially built room with Mu-metal and Aluminum. Mu-metal is an alloy of 77% nickel, 15% iron and varying amounts of copper and molybdenum, and reduces low frequency interference. The MSR reduces environmental magnetic noise so that the low brain magnetic fields can be measured. Other sources of magnetic fields come from cardiac and skeletal muscles and are in the pica Tesla range. These can be excluded by keeping the patient immobile and by timing the ECG artifact.

The MEG helmet contains the magnetic sensors, which pick up the small magnetic field on the surface of the scull. The MEG requires a temporal key and this is provided by simultaneous EEG or somatosensory evoked potential (SEP). Compared with EEG, the MEG gives better spatial resolution, is not distorted by bone, and has the same temporal resolution (5).

The tiny magnetic fields cannot be measured by ordinary means. Utilizing superconductor technology, biomagnetometers were invented. These consist of two parts: a Superconductor Quantum Interference Device (SQUID) and a Flux collector. Both the flux collector and the SQUID are bathed in a liquid helium environment at $-269^\circ$C so that superconductor physics apply. At this temperature, magnetic flux induces a current in the collector, which passes the current through a second coil at the SQUID. At the second coil the magnetic flux is converted into current and amplified. The original biomagnetometer was built in the 1970s and the first MEG scans were single channeled compared with the modern scans with 148 channels.

While MEG scan aims to record tiny cerebral magnetic fields the MRI scan, which is familiar to most anesthesiologists, is different in that it involves placing the patient in a high intensity magnetic field coil. The image is generated from the energy released from atoms subjected to radio frequency pulses in a magnetic field. The anaesthetic implications in the two environments are depicted in Table 4.

All patients referred for anaesthesia in our services were children or young adults with mild mental retardation, although the MEG environment was initially designed for adult patients. An additional consideration is that these patients are prone to convulsions and the ability to manage this complication within this environment is mandatory.

Ideally, the patient for a MEG scan should be minimally sedated, with an IV line in place and with the seizure disorder under control. In our experience, the majority of our younger patients required sedation for placement of the IV line. Because of the absence of published guidelines, initial anaesthetic management was at the discretion of the attending anaesthesiologist. After review of our initial MEG

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of failures</th>
<th>Premedication</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 ($n = 31$)</td>
<td>11 (35.5%)*</td>
<td>8 (72.7%) Midazolam</td>
<td>Propofol or sevoflurane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 (18%) Sevoflurane</td>
<td>Sevoflurane</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 (9%) Chloral hydrate</td>
<td>Midazolam</td>
</tr>
<tr>
<td>Group 2 ($n = 17$)</td>
<td>1 (5.8%)</td>
<td>1 (5.8%) Chloral hydrate and sevoflurane</td>
<td>Propofol</td>
</tr>
</tbody>
</table>

*P < 0.001 group 1 vs. group 2; group 1, nonprotocol group; group 2, protocol group.
experience and because of a high failure rate, changes were made leading to standardized anaesthetic management (chloral hydrate premedication supplemented by N<sub>2</sub>O/O<sub>2</sub>/sevoflurane if necessary for IV placement with propofol for maintenance). Our hypothesis was that chloral hydrate premedication, while allowing IV placement in satisfactory conditions would also decrease the amount of propofol needed during the procedure so enabling a higher rate of successful scans. Retrospective analysis of this experience suggests that the new standardized ‘protocol’ is superior to our previous approach, although does not guarantee a 100% success rate.

In group 1 there were 11 (35%) failures to localize ictal foci on the MEG scan. Eight of these patients (73%) received midazolam. By suppressing epileptic foci, benzodiazepines prolong the MEG scan duration and increase the likelihood of an unsatisfactory result. The doses of midazolam used may have been large enough to have an impact on the scan or may have been administered close enough to the performance of the scan to similarly affect results.

In a comprehensive review, Modica et al. (9) evaluated the pro- and anticonvulsant effects of anaesthetics. Some anaesthetics have pure proconvulsant effects (nitrous oxide, methohexital, morphine, meperidine, fentanyl, sufentanil), others are anticonvulsant (thiopental, midazolam, lorazepam), while others may have pro- and anticonvulsant effects (halothane, enflurane, isoflurane, etomidate, diazepam, ketamine, propofol, local anaesthetics).

These contradictory effects may be related to problems and differences with study designs. Factors such as patient population studied (with or without a known seizure disorder), the method of seizure activity documentation (clinical or EEG), and the type of EEG recording electrodes (surface or deep), should be considered when investigating effects of anaesthetic agents on seizure threshold (9). For example, methohexitone only produces epileptiform activity in patients with known seizure disorders (10), and fentanyl produced seizures without supportive EEG documentation (11). For certain anaesthetics such as ketamine, epileptiform activity may originate in subcortical structures, therefore, implanted depth electrodes should be used to document the ictus (12). It has also been proven that ketamine does not trigger seizure activity but, more likely, prevents seizures by N-methyl-D-aspartate (NMDA) receptor antagonism (13).

Variation in depth of anaesthesia may explain the dual convulsant effect of some anaesthetic agents (9). Although propofol decreases the duration of seizure activity during electroconvulsive therapy (14) and is used as treatment by some authors for status epilepticus (15), there have been case reports of clinical seizures, frequent spike activity on EEG, or opisthotonus after anaesthesia with propofol (16, 17). Cheng found that large doses of propofol (5.7 ± 2.6 mg·kg<sup>−1</sup>) caused burst suppression on electrocorticography (18). This raises the supposition that a deeper level of propofol anaesthesia might prevent localization of the ictus foci in some patients,
while lighter levels would not disturb the MEG scanning. The total doses of propofol in the two groups were not significantly different, although it is possible that higher doses at a particular time had an inhibitory effect on the electrocorticography. We could not validate our assumption that the total propofol dose used in children receiving chloral hydrate premedication would be less than the propofol dose used without chloral hydrate.

Chloral hydrate provided an acceptable level of sedation for IV placement in 76% of the patients in group 2 (23% required supplemental sevoflurane anaesthesia). Chloral hydrate has been successfully used by some authors in treatment of status epilepticus or refractory epilepsy (19).

The use of sevoflurane in epileptic patients is controversial. Sevoflurane suppresses central nervous system background activity, but in animal experiments, deep anaesthesia activates the EEG (20). Sevoflurane has neurophysiological properties similar to enflurane and increases the EEG and SEP responses to high-frequency electrical stimulation of the skin or brain stem. In addition, EEG evidence of seizure activity during deep sevoflurane anaesthesia has been seen in patients known to have epilepsy (21). Seizures following sevoflurane anaesthesia have been reported in the literature (22). Additionally, sevoflurane anaesthesia is associated with agitation during induction and postoperatively, although agitation observed during sevoflurane induction does not seem to be associated with seizures (23). Given these considerations, sevoflurane was only used for a short period to facilitate IV access in situations in which chloral hydrate was not successful (23% of patients in group 2).

In four cases, clonidine was used for premedication, as it induces both sedation and epileptiform discharges in patients with localization-related epilepsy (24). The availability of only a 0.150 mg tablet makes oral dosing difficult in children. All four cases yielded a successful scan. The use of dexmedetomidine, a titrable short-acting alpha 2 agonist, may be another option, and has been reported to have proconvulsant actions (25).

In conclusion, we report the first anaesthesia experience with MEG in children with intractable seizures. Use of midazolam in this setting is associated with a high (73%) failure rate of interictal activity and localization. Future studies should evaluate chloral hydrate as premedication, the optimal dose of propofol, the minimal alveolar concentration of volatile anaesthetic needed (if used) and the potential benefit of agents such as dexmedetomidine.

References

2. Ebersole JS. Magnetoencephalography/Magnetic Source Imaging in the assessment of patients with epilepsy. Epilepsia 1997;38(Suppl. 4):S1–S5.


Accepted 28 May 2003