Intraoperative monitoring of somatosensory evoked potentials (SSEP) is used increasingly during central nervous system surgery to improve intraoperative monitoring of neural tracts at risk. Monitoring of these potentials is made difficult by technical, physiological, surgical and anaesthetic changes which may cause alterations in neural function. Anaesthetic agents can produce dramatic alterations in SSEP which may mimic neural injury. This is of particular concern at the beginning of the anaesthetic, when marked physiological changes and positioning may place neural structures at risk before surgery.

Several studies have demonstrated alterations in SSEP with various anaesthetic agents. Many of these changes are dose-related [1] in a manner similar to dose-related effects on the electroencephalogram (EEG). Few studies have examined carefully the time-related effects of these agents. If an effect on SSEP is based on an anaesthetic effect, the alteration should be consistent with the time course and known method of action of the agent. Studies of the effect of thiopentone on the EEG show a time course similar to anaesthetic effect [2].

Thiopentone is a commonly used induction agent that has been shown to alter SSEP, but a careful time-related study of induction doses has not been conducted. This study was designed to examine the time course of SSEP effects of an induction bolus of thiopentone on the median nerve SSEP.

**SUMMARY**

We have studied the effects of an i.v. bolus of thiopentone 4 mg kg⁻¹ on the median nerve somatosensory evoked potentials (SSEP) in 15 unpremedicated patients. The latency and amplitude of the SSEP response over the second cervical vertebra (SC) and sensory cortex (P₁₅, N₂₀, P₂₅) were recorded before and for 12 min after injection. Data were analysed at 0, 4, 8 and 12 min for time-related alterations. Cortical amplitude was variable, with a tendency to decrease (P < 0.03). There was a statistically significant but clinically insignificant transient increase in latency of the cortical N₂₀ (P < 0.008), and interwave conduction times of SC to P₁₅ (P < 0.007) and SC to P₂₅ (P < 0.039). The relation of these results to the proposed mechanism of thiopentone action at synapses is discussed.

**PATIENTS AND METHODS**

Fifteen ASA Class I and II patients scheduled to undergo thoracic or lumbar spinal surgery with SSEP monitoring gave written informed consent to participate in this study, which was approved by the Institutional Review Boards. Patients with possible neurological abnormalities in the median nerve pathway or intracranial pathology were excluded.

Unpremedicated patients came to the operating room where a catheter was inserted into a vein and the overnight fluid deficit was replaced over 30 min using 2.0 ml kg⁻¹ h⁻¹ of 5% dextrose in lactated Ringer’s solution. Routine anaesthesia monitoring included precordial stethoscope, spirometer, continuous electrocardiogram, automated arterial pressure, temperature and endtidal carbon dioxide measurement.

Disc recording electrodes with electrode paste
were attached with collodion after skin abrasion. The active electrode for cortical recording was placed over the primary somatosensory cortex for the arm being stimulated, 2 cm posterior to C₃ (right hand) or C₄ (left hand), with the reference electrode at F₁ (International 10–20 system). The active electrode for cervical recording was placed at the inion (SC) with F₁ as the reference electrode. A silver–silver chloride ground electrode was placed on the shoulder. All electrode impedances were less than 3000 Ω, and channel electrodes were matched within 1000 Ω. Median nerve SSEP were obtained using stimulation at the wrist with a bipolar bar electrode following application of electrode gel and gentle skin abrasion. Constant current stimulation using 300-μs square wave impulses was used at 5.7–8.7 Hz at a current 1 mA greater than that sufficient to produce a motor response.

For each averaged waveform, 250 artefact free responses were obtained using a Nicolet Pathfinder II or Nicolet CA-1000/DC-2000 signal averager (Nicolet Biomedical, Madison, Wisconsin), using bandpass filtration of 5–250 Hz (60 Hz notch filtration was not used) and an analysis window of 50 ms. All acquired data were stored on magnetic discs for later analysis.

After satisfactory duplicate baseline recordings were obtained, thiopentone 4 mg kg⁻¹ was given i.v. over 30 s. The SSEP, arterial pressure (AP) and heart rate (HR) were recorded every 1 min after the dose, and ventilation of the lungs was assisted manually as necessary with a facemask using 40% oxygen in air to maintain end-tidal carbon dioxide partial pressure at 4.7–6.0 kPa. All patients had a body temperature exceeding 36.5 °C at the conclusion of the study. SSEP data were acquired at 1-min intervals for 9 min, and then every 3 min until 30 min after injection. The patients then received an opioid-based anaesthetic (sufentanil or fentanyl) supplemented with 0.4% isoflurane or an infusion of thiopentone 1.5 mg kg⁻¹ h⁻¹ before tracheal intubation and surgery. Posterior tibial nerve SSEP were monitored during surgery.

Data from the waveforms were acquired after the study by recall of stored averages. Post-stimulus latency of the major cervical negative wave (SC) (approximately 15 ms) and the latencies of the primary cortical response waves (P₁₅, N₂₀ and P₂₅) were recorded. The conduction times (CT) were calculated as intervals between various peaks. Cortical amplitude was taken as the voltage from the N₂₀ trough to the P₂₅ peak of the cortical response.

SSEP latencies, conduction times, amplitudes and physiological variables (arterial pressure and heart rate) at 0, 4, 8 and 12 min were compared using Friedman two-way analysis of variance; differences were confirmed with the Wilcoxon matched pairs signed ranks test. Statistical significance was considered when P < 0.05.

RESULTS

We studied seven women and eight men, mean age 42 yr (range 18–81 yr), average height 172 cm (range 157–185 cm) and weight 72 kg (range 49–90 kg). No patient had a haemoglobin concentration less than 3.5 g dl⁻¹ or serum albumin concentration less than 11.7 g dl⁻¹. All patients tolerated the study well. Most patients were awake by 15 min from induction. By 18 min, 12 patients had recording of the SSEP stopped because they were awake or moving extremities such that further recordings could not be taken.

Only one patient did not awaken during the 30 min. Inadequate tracings beyond 12 min precluded study at later times. Figure 1 shows selected tracings of the cervical and cortical response of one patient in whom recordings were acceptable for 12 min. No patient expressed unpleasant recall of the study period.

There was no difficulty obtaining the post-stimulus latencies immediately after the bolus of thiopentone. A statistically significant change in latency (P < 0.008) occurred in the cortical N₂₀ response (table I). Examination of figure 1 and assessment by Wilcoxon analysis demonstrated a significant difference between time 0 and later times, confirming the impression that the increase occurred quickly after injection (1–2 min) and resolved during the study period. However, the absolute latency increase was small. Changes in the latencies of the other cortical peaks were also small and not statistically significant.

Analysis of the interwave latencies between peaks (conduction times) revealed significant differences between the cerebral response and cortical P₁₅ (P < 0.01) and between the cerebral response and cortical P₂₅ (P < 0.05). Again, the major change occurred shortly after injection. As with the absolute latencies, the conduction time changes were small.

Baseline amplitudes ranged from 0.7 to 6.3 μV. The individual response of amplitude to thio-
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Fig. 1. SSEP responses recorded from the cervical and cortical electrodes as detailed in the text, before (0) and at 10 times following the injection of thiopentone in one patient. Cervical spinal cord response (SC): negative response at the active electrode is upward. The peaks evaluated in the cortical response (P_{15}, N_{20}, P_{25}) are indicated: positive response at the active electrode is shown upward.

TABLE I. Effects of thiopentone on SSEP latency and amplitude and cardiovascular variables (mean (SD)). One patient was excluded from analysis at 12 min only. *P < 0.05

<table>
<thead>
<tr>
<th>Latency (ms)</th>
<th>Baseline</th>
<th>4 min</th>
<th>8 min</th>
<th>12 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC</td>
<td>15.54 (1.59)</td>
<td>15.34 (1.51)</td>
<td>15.48 (1.61)</td>
<td>15.48 (1.49)</td>
</tr>
<tr>
<td>P_{15}</td>
<td>17.35 (1.43)</td>
<td>17.91 (1.83)</td>
<td>18.06 (1.59)</td>
<td>17.91 (1.94)</td>
</tr>
<tr>
<td>N_{20}</td>
<td>20.79 (1.79)</td>
<td>21.68 (2.22)</td>
<td>21.69 (2.08)</td>
<td>21.61 (2.62)</td>
</tr>
<tr>
<td>P_{25}</td>
<td>25.47 (2.57)</td>
<td>25.85 (3.38)</td>
<td>25.53 (2.94)</td>
<td>25.89 (3.00)</td>
</tr>
</tbody>
</table>

| Amplitude (µV) | N_{1}-P_{2} | 3.51 (1.93) | 2.67 (1.79) | 2.78 (1.75) | 2.46 (1.41) |
| Physiological variables | SAP (mm Hg) | 133 (16) | 120 (16) | 121 (17) | 120 (17) |
|                  | DAP (mm Hg) | 85 (12) | 77 (14) | 75 (11) | 75 (13) |
|                  | HR (beat min^{-1}) | 77 (11) | 79 (13) | 74 (4) | 73 (11) |

Pentone was variable; however, the mean amplitude of all patients tended to decrease significantly and outlasted the period of hypnosis produced by the drug (P = 0.03) (table I). There did not appear to be any relationship between amplitude or latency and awakening time.

There were significant changes in systolic and diastolic arterial pressure (P < 0.0008 and P < 0.012, respectively), but not in heart rate or pulse pressure (table I).

DISCUSSION

This study has demonstrated that thiopentone altered the short latency median nerve SSEP responses during at least the first 12 min after induction of anaesthesia in unpremedicated patients. The most marked change was a reduction in cortical amplitude; however, the early response was variable. Although significant for some values, the absolute degree of change of latency values was small.
Variability of cortical amplitude has been reported in other studies in animals and man. An eventual decrease in amplitude after thiopentone has been observed consistently [3,10]. In these studies, the final stabilization of this amplitude effect was observed by 6-9 min [5], 12-15 min [6] or 30 min [6]. This is consistent with our study, in which stabilization of the amplitude occurred usually by 3-10 min.

The latency changes seen are also consistent with previous studies which demonstrated marked alteration in late cortical peaks with minimally altered early responses [3,7-11]. The increase in latency of cortical peaks was exaggerated with later peaks (table I). This progressive effect at later latency has been observed by Angel, Berridge and Unwin [6], Clark and Rosner [12] and Shaw and Cant [13] and has been suggested as consistent with an effect of barbiturates on synaptic transmission [4]. The assessment of late cortical peaks in this study is limited because of the high rate of stimulation.

Alterations in physiological variables associated with i.v. injection of thiopentone observed in this study are similar to those reported by others [14-18]. It is unlikely that the change in heart rate or decrease in arterial pressure are responsible for the amplitude and latency alterations, as the absolute magnitude of AP and HR changes was small. As body temperature and end-tidal carbon dioxide partial pressure were maintained constant, the changes observed were probably related to neural effects of the barbiturate.

It is notable that stabilization of the evoked potential changes occurred at a time similar to the stabilization of cardiovascular changes. This may suggest that the haemodynamic and cerebral events were consequences of drug delivery and dependent on drug concentrations at the effector sites. The early onset of these SSEP changes, as with the physiological variables, is consistent with the predicted delivery of thiopentone to the central nervous system within 1 min after i.v. injection [19].

A lack of correlation between time of awakening and the measured parameters of the evoked potentials was observed also in a study of drug-free schizophrenics given thiopentone [6]. It is of interest that the changes in latency and amplitude persisted beyond awakening. The effect is consistent with the known phenomena of acute tolerance [20]. Alternatively, the drug–effector interaction at the pathways of wakefulness may operate via a different mechanism.

Although the data reported here are generally consistent with previous reports, there are small differences between this study and other studies cited. In general, these differences concern latency changes in the lateral cortical peaks. Whereas some differences may relate to specific species, doses or barbiturate used, differences could result from the measurements used: the stimulating and recording variables used in this study are those used routinely by the authors, but differ from several of the studies cited. The high rate of stimulation limits assessment of late cortical peaks. Further, the choice of active recording sites may influence the recording of waves which could be recorded optimally at different locations (particularly late cortical waves).

All these patients had easily monitored evoked responses during the study period and for the remainder of the surgical period. This confirms the clinical impression that evoked response monitoring can be conducted following induction with thiopentone. However, as the amplitude of the cortical response is reduced, neural insults related to positioning or induction would be detected best by excessive latency change or alterations after the initial period of instability.

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REFERENCES


