EFFECTS OF ISOFLURANE ANAESTHESIA ON THE MEDIAN NERVE SOMATOSENSORY EVOKED POTENTIAL IN CHILDREN†

D. G. MASON, D. HIGGINS, S. G. BOYD AND A. R. LLOYD-THOMAS

SUMMARY

Evoked potentials are used to determine the integrity of neural pathways during neurosurgical and orthopaedic procedures, but the extent to which they may be altered by anaesthetic agents has not been studied systematically in children. In this study we have recorded median nerve somatosensory evoked potentials (mnSSEP) in children during isoflurane anaesthesia to determine if there are changes similar to those seen in adults. We studied 10 patients using standardized anaesthetic and clinical neurophysiological techniques. Control mnSSEP were obtained with 70% nitrous oxide in oxygen and isoflurane was then administered at 0.25, 0.50 and 0.75 MAC. The latencies and amplitudes of the mnSSEP were subjected to repeated measures analysis of the variance (ANOVA) and linear regression. There were statistically significant increases in N20, P22 latencies and central conduction time (P < 0.001) and reductions in amplitude of the N20-P22 complex (P < 0.03) with increasing end-tidal isoflurane concentrations. These results are similar to the findings in adults. (Br. J. Anaesth. 1992; 69: 562–566)

KEY WORDS


Evoked potentials have been extensively investigated during anaesthesia [1]. Graded changes in latencies and amplitudes of the early cortical components of the somatosensory, auditory and visual evoked potentials occur with increasing end-tidal concentrations of inhalation agents in adults [2–6]. These have been proposed as an objective measurement of depth of anaesthesia in the prevention of awareness [7, 8].

Although evoked potential techniques are now used increasingly in anaesthetized children to determine the integrity of neural pathways during neurosurgical and orthopaedic procedures, no substantive study has been performed of the associated effects of anaesthesia on the evoked potentials in children. Measurement of evoked potentials in children is technically more difficult than in adults, and in commencing this investigation of the effect of these agents in young children the median nerve somatosensory evoked potential (mnSSEP) was chosen. This produces a robust, large-amplitude response which seemed more suitable for this study than middle latency auditory evoked potentials, which have been used in adult work, but which are inconsistently recordable in young children [9, 10]. The aim of our study was to determine the effects of isoflurane in nitrous oxide and oxygen on the latencies and amplitudes of the mnSSEP in children.

PATIENTS AND METHODS

After Ethics Committee approval, informed consent was obtained from the parents or guardians of 10 children aged between 10 months and 6 yr (mean 3 yr) presenting for surgery for repair of hypospadias. All patients were ASA I, with no known neurological deficit. All patients received a standard anaesthetic which was administered by a person who was not a project team member.

The children were premedicated 90 min before surgery with trimetaphazine 4 mg kg⁻¹ and atropine 0.04 mg kg⁻¹ orally (this investigation was undertaken before the maximum recommended dose of trimetaphazine was reduced to 2 mg kg⁻¹). Anaesthesia was induced with 3% halothane and nitrous oxide in oxygen and oral tracheal intubation was performed after i.v. administration of atracurium 0.5 mg kg⁻¹. Anaesthesia was maintained with 70% nitrous oxide in oxygen and caudal extradural anaesthesia with 0.25% bupivacaine 0.5 ml kg⁻¹. Positive pressure ventilation was used with a Siemens 900B ventilator at 12 b.p.m. to achieve an end-tidal carbon dioxide concentration of 5%. ECG, SPO₂, FIsO₂, FIsN₂, and nasopharyngeal temperature were recorded. End-
ISOFLURANE ANAESTHESIA AND EVOKED POTENTIALS IN CHILDREN

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TABLE I. Recording techniques for mnSSEP in children

<table>
<thead>
<tr>
<th>Stimulation variables</th>
<th>Recording variables</th>
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<tr>
<td>Site</td>
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<tr>
<td>Electrodes</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Type</td>
<td>Band width</td>
</tr>
<tr>
<td>Intensity</td>
<td>Repetitions per run</td>
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<tr>
<td>Duration</td>
<td>Pre-stimulus analysis</td>
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<tr>
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<tr>
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<tr>
<td></td>
<td>Reference: frontal</td>
</tr>
<tr>
<td>2</td>
<td>Reference: cervical</td>
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<td>3</td>
<td>Reference: frontal</td>
</tr>
<tr>
<td></td>
<td>Reference: ipsilateral ear</td>
</tr>
<tr>
<td></td>
<td>Active: left parietal</td>
</tr>
</tbody>
</table>

Right median nerve at wrist
Percutaneous disc electrodes
Direct current
75 "volts"
0.2 ms
270 ms

Digitimer D200
100 µV V⁻¹
30 ms (time constant) to 3 KHz
275
20 ms
55 ms
Silver–silver chloride
< 3000 Ω
Collodion fixation and electrode conduction gel

The mnSSEP were measured using a standard technique with a Digitimer D200 (Digitimer Ltd, Welwyn Garden City, Hertfordshire, England) (table I). All data were stored on a floppy magnetic disk and analysed off-line. The EEG signal from the active left parietal electrode referred to a right parietal electrode was recorded continuously onto magnetic tape and was processed by the Cerebral Function Analysing Monitor (CFAM). This arrangement allowed us to monitor both the EEG signal quality and the effects of anaesthesia. Evoked potential recordings contaminated by electrical interference from diathermy were rejected.

After non-stimulus controls, the measurement of mnSSEP was commenced 20 min after induction of anaesthesia, thus ensuring that the halothane had cleared, as confirmed by vapour analysis using the Datex Capnomac. Evoked potentials were recorded every 90–180 s until completion of the study. Six control mnSSEP were recorded before the start of surgery and isoflurane was introduced in a stepwise fashion to reach end-tidal concentrations equivalent to 0.25, 0.50 and 0.75 MAC, corrected for each child’s age, but without a correction for the presence of nitrous oxide [11]. The required end-tidal isoflurane concentration was achieved using over pressure and was held constant for 15 min at each concentration.

Analysis of the mnSSEP was conducted off-line. The latencies from the stimulus to the N13, N20 and P22 components of the mnSSEP were measured and the central conduction time (CCT) (N20–N13) was derived. The peak amplitude of N13 was measured from the pre-stimulus baseline, while the amplitude of the N20–P22 complex was measured peak-to-peak. When the electrical stability of the mnSSEP had been achieved at each end-tidal concentration, the mean amplitudes and latencies were derived.

![Fig. 1. Effects of isoflurane in 70% nitrous oxide in oxygen on the mnSSEP of patient No. 3, showing increasing latency and reduction of amplitude of the N20–P22 complex with increasing concentrations of isoflurane. For each measurement, four consecutive evoked potentials are superimposed.](image-url)
from four successive evoked potentials. Data were analysed using repeated measures analysis of the variance (ANOVA) and linear regression [12].

RESULTS
Satisfactory mnSSEP were recorded in all children; figure 1 illustrates the effect of isoflurane on the evoked potentials obtained from patient No. 3. The

TABLE II. Effects of isoflurane in 70% nitrous oxide in oxygen on the mean (sd) latencies of the mnSSEP in 10 children. *** P < 0.001

<table>
<thead>
<tr>
<th></th>
<th>N13</th>
<th>N20</th>
<th>CCT</th>
<th>P22</th>
</tr>
</thead>
<tbody>
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<td>70% N2O</td>
<td>7.49</td>
<td>15.64**</td>
<td>8.15**</td>
<td>22.14***</td>
</tr>
<tr>
<td>in oxygen</td>
<td></td>
<td>(0.78)</td>
<td>(1.36)</td>
<td>(1.56)</td>
</tr>
<tr>
<td>0.25 MAC</td>
<td>7.50</td>
<td>16.92***</td>
<td>9.42***</td>
<td>23.78***</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(0.78)</td>
<td>(1.74)</td>
<td>(1.88)</td>
</tr>
<tr>
<td>0.50 MAC</td>
<td>7.50</td>
<td>18.23***</td>
<td>10.79***</td>
<td>26.20***</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(0.78)</td>
<td>(2.06)</td>
<td>(1.95)</td>
</tr>
<tr>
<td>0.75 MAC</td>
<td>7.51</td>
<td>19.45***</td>
<td>12.04***</td>
<td>28.40***</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(0.77)</td>
<td>(2.56)</td>
<td>(2.40)</td>
</tr>
</tbody>
</table>

TABLE III. Effects of isoflurane in 70% nitrous oxide in oxygen on the mean (sd) amplitudes of the mnSSEP in 10 children. * P < 0.03

<table>
<thead>
<tr>
<th></th>
<th>N13</th>
<th>N20-P22 (Fz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70% N2O</td>
<td>3.85</td>
<td>3.34*</td>
</tr>
<tr>
<td>in oxygen</td>
<td></td>
<td>(1.98)</td>
</tr>
<tr>
<td>0.25 MAC</td>
<td>3.63</td>
<td>2.53*</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(2.10)</td>
</tr>
<tr>
<td>0.50 MAC</td>
<td>3.93</td>
<td>2.98*</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(2.58)</td>
</tr>
<tr>
<td>0.75 MAC</td>
<td>3.44</td>
<td>1.60*</td>
</tr>
<tr>
<td>isoflurane</td>
<td></td>
<td>(2.03)</td>
</tr>
</tbody>
</table>

mean arterial pressure did not alter more than 15% in any patient. Nasopharyngeal temperatures were within 0.5 °C of control values in all patients.

In the presence of isoflurane there were significant differences in the grouped data between N13, N20 and P22 latencies and the CCT (P < 0.001, ANOVA) (table I). Comparing the slopes of latency against isoflurane concentration among the patients, there was no significant change in N13 latency with
increasing concentrations of isoflurane. However, with N20, P22 and CCT there were significant increases in latency proportional to increasing concentrations of isoflurane ($P < 0.001$) (fig. 2).

There were significant differences in the response to isoflurane between N13 and N20–P22 amplitudes ($P < 0.05$, ANOVA) (table III, fig. 3). Comparing the slopes of amplitude against isoflurane concentration among the patients, there were no significant changes in the N13 amplitude with increasing concentrations of isoflurane. There were significant reductions in N20–P22 amplitude which were proportional to increasing concentrations of isoflurane ($P < 0.03$).

**DISCUSSION**

The aim of this study was to develop a technique for monitoring mnSSEP during anaesthesia in children, thus providing reference values for the effects of isoflurane on these potentials and enabling comparison with similar investigations in adults.

There are several factors not related to anaesthesia which may have influenced the results. The amplitude and latency of the mnSSEP are affected by age, body temperature, mean arterial pressure, end-tidal carbon dioxide concentration and surgical stimulation. The latencies of the mnSSEP in children are shorter than comparable potentials in adults, mainly because of differences in height. The expected N20 latency of children between the ages of 10 months and 6 yr is 15.7 (SD 0.94)–15.52 (0.54) ms [13]. The use of collective data in children with a wide age range may result in a large variance; although a large variance did occur, highly significant changes in latencies and amplitudes occurred at different fractional MAC of isoflurane. The changes in temperature and mean arterial pressure were not sufficient to affect the evoked potentials. Surgical stimulus is known to oppose the effect of inhalation agents on the latencies and amplitudes of the mnSSEP [14]; in this study, this effect was eliminated by the use of caudal extradural analgesia. This was confirmed by the absence of change in the cardiovascular variables in response to surgery or evoked potential recording and by the fact that all the patients had satisfactory analgesia at the end of the operation. In addition, observation of the CFAM traces showed no evidence of arousal responses during surgery [15].

Early investigations of evoked potentials during anaesthesia in animals and adult humans showed that increases in latency and reduction in amplitude of the cortical components occurred [16, 17]. More recent investigations have shown that these changes are graded to changes in end-tidal anaesthetic concentration [2–4, 18]. Most of the studies have involved a single inhalation anaesthetic agent; this investigation follows routine clinical anaesthesia in children using a balanced anaesthetic technique, including nitrous oxide in oxygen as background anaesthesia. Control measurements were taken after induction of anaesthesia in the presence of 70% nitrous oxide in oxygen; this may have reduced the absolute amplitude of mnSSEP, but probably had little effect on the latency [19]. As the end-tidal nitrous oxide concentration remained constant throughout the investigation, it seems reasonable to attribute any changes which occurred in the mnSSEP to different end-tidal concentrations of isoflurane.

This study has demonstrated in children, as in adults, that there were dose related changes in the N20 and P22 components of the mnSSEP with increasing end-tidal concentrations of isoflurane [2–4]. In addition, we have shown a differential effect of isoflurane on the central nervous system as the increase in CCT can be accounted for by the changing latency of the N20. Although changes in the amplitude of the N20–P22 complex were recognized easily on visual inspection of the traces, they were difficult to quantify. This may have been a result of several factors, but is most likely to be as a result of technical difficulties in defining a baseline reference point for measurement. These findings support the views of Samra and co-workers, who suggested that latency provided the better measure of anaesthetic effects on the mnSSEP [2].

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**REFERENCES**

**Original Text**

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