Memory for auditory material presented during anaesthesia

C. J. R. Parker, J. D. L. Oates, A. H. Boyd and S. D. Thomas

SUMMARY

We have assessed postoperative memory for lists of 10 neutral words, presented by tape recording, in patients anaesthetized by a standardized technique comprising thiopentone 5 mg kg\(^{-1}\), midazolam 0.07 mg kg\(^{-1}\), fentanyl 3 \(\mu\)g kg\(^{-1}\) and 70% nitrous oxide in oxygen, using both free recall and a test in which the subject was asked to indicate the presented words from a larger list. Twenty-four patients were exposed to one of four tape-recorded lists of words and 24 were presented with a blank tape. There was no instance of free recall of presented words. Analysis of the responses in the implicit memory test revealed no difference between the performance of the patients who had been exposed to a word list and those who had not. (Br. J. Anaesth. 1994; 72: 181–184)

KEY WORDS


After the widespread adoption of neuromuscular blocking drugs in anaesthetic practice, it was recognized that the use of these agents together with light anaesthesia may allow postoperative recall of intraoperative events; furthermore, some patients report intraoperative dreaming of a distressing nature [1]. The phenomena of intraoperative awareness and distressing dreams can be abolished by the use of a small inspired concentration of a volatile anaesthetic agent [2].

There remains doubt, however, if the absence of recall implies that intraoperative stimuli are neither appreciated nor without effect. There are two main approaches to this problem. One is to attempt to establish verbal communication with the anaesthetized patient with the aid of one arm isolated from the action of the neuromuscular blocking drug by use of a tourniquet, allowing the patient to move that limb in response to a command [3, 4]. The second is to use more refined techniques to establish the presence of memory for material presented during operation. These include the use of postoperative hypnosis [5]; the observation, after operation, of specific motor behaviour suggested to the patient during operation [6]; and implicit tests of memory for verbal material [7, 8]. It is unfortunate that, in some of these studies, the anaesthetic was not standardized, either in choice of drugs or dosage used. In addition, such studies, which have used a variety of methods of testing implicit memory, have yielded a confusing mixture of positive [7] and negative [8] results.

Performance in some implicit memory tests, such as word completion, is spared after use of benzodiazepines in conscious subjects [9]. The purpose of the present study was to attempt to evaluate memory formation during a standardized anaesthetic including the widely used benzodiazepine, midazolam; a similar anaesthetic technique is used often in studies to evaluate pharmacodynamics of neuromuscular blocking drugs. The design of the study closely followed that adopted by Millar and Watkinson in 1983 [7], who obtained a positive result using postoperative testing for memory of words presented during operation, but failed to standardize the anaesthetic regimen, using halothane in varying concentrations in about 75% of their patients.

PATIENTS AND METHODS

The study was approved by the Ethics Committee of the Royal Liverpool University Hospital. We studied 48 patients undergoing minor or intermediate surgery requiring neuromuscular block. The patients were visited on the evening before surgery and were told that there is some evidence that information played to anaesthetized patients may be retained in the memory. Written informed consent was obtained to play a tape recording during surgery, which might contain some words or might be blank and to complete a simple test on the next day which would involve listening to a tape recording of some words and indicating which they thought had been played.

Patients were excluded if they were taking regular psychotropic medication or had a history of a hearing disorder. Hearing was not tested formally and auriscope examination was not undertaken.

Eight tapes (TDK D60), labelled with a letter A–H, were used. After entry to the study, each patient was randomly assigned a tape from a previously sealed envelope. Four of these were blank (the control group) and four contained a series of 10 words, taken from 31 categories of Battig and Montague category norms [10], with an average rank of 20.2 (SD 3.4). Categories included, for example: type of tree, type of fish; category exemplars included, for example: willow, mackerel. Each word appeared...
on only one tape. The words were read at the rate of one word every 2 s and repeated in a different order four times; this sequence was then repeated for a total duration of 20 min.

Premedication comprised diazepam 10 mg orally, given between 1.5 and 4 h before the start of surgery. When the patient arrived in the anaesthetic room, a vein was cannulated and headphones (Sony MDR-005) attached to the patient. After it had been ascertained that the headphones were comfortable, a tape recording of music was played, and the volume adjusted to suit the patient. The music was stopped and midazolam 0.07 mg kg\(^{-1}\) given i.v. with fentanyl 3 \(\mu\)g kg\(^{-1}\). After 3–5 min, anaesthesia was induced with thiopentone 5 mg kg\(^{-1}\) and neuromuscular block produced with atracurium 0.6 mg kg\(^{-1}\). Ventilation of the lungs was controlled manually with 70% nitrous oxide in oxygen and the trachea intubated when appropriate. Thereafter, mechanical ventilation was established to maintain an end-tidal carbon dioxide partial pressure of 4.0–4.7 kPa. No volatile anaesthetic agent was used.

The tape was started when surgery began. During the operation, further increments of fentanyl 50 \(\mu\)g and atracurium were given as clinically indicated. After the end of surgery, residual neuromuscular block was antagonized with a mixture of neostigmine 2.5 mg and atropine 1.2 mg, spontaneous ventilation was re-established, and the trachea extubated when appropriate. The headphones were then removed.

The postoperative interview was conducted on the morning of the first day after operation, between 16 and 24 h after the start of surgery, by an interviewer who was unaware which tape the patient had been played.

After a preliminary conversation in which the patient was asked about the presence of postoperative symptoms including pain, the patient was reminded that s/he had been played a tape recording while anaesthetized, and was asked if any words came to mind (free recall). The patient was then given a printed list of the 40 words used on all four tapes; the words on this list were ordered such that the words from the four tapes were randomly interspersed. Simultaneously, a tape recording in which these words were read (about one word every 2 s) was played, and the patient was asked to indicate which words s/he thought had been presented during surgery, and to guess if necessary; the choice was indicated by marking the printed list.

After completion of this task, the subject was asked if he or she felt confident about the response to any of the words on the list, or if the response was speculative.

For the purpose of analysis, each tape containing words was paired with a blank tape. When the patient indicated, in the postoperative test, a word which was on the tape s/he had been played in theatre, or when s/he had been played the blank tape paired with that tape, the response was scored as a "hit". When the patient indicated a word which was not on the tape s/he had been played, or when s/he had been played a blank tape paired with one on which the word did not appear, the response was scored as a "false alarm". From the rates of hits and false alarms, a non-parametric estimate of signal sensitivity (\(P(A')\)) was calculated [11]. This is a measure of the sensitivity of the subject in making the decision as to whether a word had been played, taking account of both correct and incorrect responses. A value of 0.5 indicated a performance based upon chance and a value of 1 indicated a perfect distinction between signal and noise. Statistical comparisons between groups were made using the Mann–Whitney \(U\) test, and correlations evaluated using the Spearman rank correlation coefficient.

**RESULTS**

The experimental and control groups were comparable with regard to age, weight and gender (table I). The duration of surgery ranged from 29 to 183 min; the groups were comparable in this respect and formal testing did not reveal a significant difference (Mann–Whitney \(U = 241.5; n = 24\) in each group; \(P > 0.05\)).

At the postoperative visit, none of the patients had spontaneous recall of any words (table II).

The total response rate was greater in the experimental group, but this difference did not reach statistical significance (\(P > 0.1\)). The rates of correct response (hits) and incorrect response (false alarms) reflected the overall response rate, and were not significantly different in either group. The mean value of \(P(A')\) was not significantly greater in the experimental group than in the control group (\(P > 0.1\)).

Of the 24 patients in the experimental group who were presented with verbal material, 11 required incremental doses of fentanyl (50 \(\mu\)g in six, 100 \(\mu\)g in two, 150 \(\mu\)g in two cases and 200 \(\mu\)g in one). Among the patients in the experimental group, \(P(A')\) was not correlated significantly with either the total in-

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<tr>
<th>TABLE I. Physical characteristics of the patients studied and duration of surgery (mean (SD) [range] or number)</th>
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<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
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<tr>
<td>41.9 (32.1)</td>
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<tr>
<td><strong>Weight (kg)</strong></td>
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<tr>
<td>[43–90]</td>
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<td><strong>Sex (M: F)</strong></td>
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<td><strong>Duration of surgery (min)</strong></td>
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<td>[30–183]</td>
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<th>TABLE II. Results of postoperative testing, expressed as total number of responses, number of correct responses (hits) and number of incorrect responses (false alarms), together with the derived values of (P(A')) (mean (SD) [range]). No significant difference between groups (Mann–Whitney rank sum test)</th>
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<tbody>
<tr>
<td><strong>Experimental</strong></td>
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<tr>
<td><strong>Total responses</strong></td>
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<td>[1–19]</td>
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<td><strong>Hits</strong></td>
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<td><strong>False alarms</strong></td>
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<td><strong>P(A')</strong></td>
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incremental dose of fentanyl used (Spearman rank correlation coefficient = 0.06; \( n = 24; P > 0.05 \)) or the duration of surgery (Spearman rank correlation coefficient = 0.09; \( P > 0.05 \)).

With four exceptions, the patients attributed their performance in the formal task to guesswork. Of the four exceptions, each patient named one word which they believed had been played to them. In two cases the choice was correct. In one instance the patient had been played a blank tape, and in one instance the word stated was not on the tape played.

**DISCUSSION**

The main finding of the present study was the failure to demonstrate either free recall, or implicit postoperative evidence of memory, of material presented during operation. While the present study may be too small to exclude the possibility of memory preservation, the results contain no suggestion of any trend to that effect. Furthermore, the analysis of the present data used the methods of signal detection theory, which considers incorrect responses and correct ones, in order to provide a sensitive measure of stimulus detection [7, 11].

It is clear that memory is not a single phenomenon, but that different categories of memory function may be defined by different techniques. A broad distinction may be drawn between explicit memory, in which the subject consciously experiences remembering, and implicit memory, in which the evidence for the memory is based on altered behaviour [12]. The memory categories differ in their properties, including their response to drugs. In particular, tests of implicit memory have been found to be less dependent upon the attention of the subject [13] and to be relatively spared by benzodiazepines in conscious subjects [9, 14]. The distinction is, however, phenomenological rather than mechanistic; the different memory categories are defined in terms of test performance, not as distinct neurological substrates. The memory sought in the present study, based on speculation as to what words a patient was exposed to, without a conscious memory of their exposure, comes within the implicit category.

The present results contrast with some others, notably with those of Millar and Watkinson [7], who found evidence of implicit memory in a study of similar design, although with a less standard anaesthetic technique and including the use of a volatile anaesthetic agent, and those of Stolzy, Couture and Edmonds [15], who used premedication with i.v. diazepam and anaesthesia with 50% nitrous oxide in oxygen supplemented by an unstated end-tidal concentration of isoflurane. In addition, Stolzy's group scored only correct responses and did not take account of false alarms, reducing the sensitivity of the analysis. The same group subsequently obtained negative results using a similar experimental paradigm in patients anaesthetized with diazepam, fentanyl and nitrous oxide [16].

A survey of more recent studies in this area reveals a mixture of positive [6, 17–21] and negative findings [8, 21, 22]. The factors which lead to a positive result are still not clearly defined.

The time of postoperative testing has varied widely among studies. Positive results have been obtained when testing for memory of verbal material was conducted as early as 3 h after surgery [17], and for specific motor behaviour as late as 20 days [18]. Both Millar and Watkinson [7] and Stolzy, Couture and Edmonds [15] conducted the postoperative test within the first 2 days after surgery, and it seems unlikely that the present negative result could be attributed to the time of testing.

The present study did not attempt to enhance the saliency of the intraoperative material for the patient, for example by including in the tape recording an instruction that the message is very important, as was done by Millar and Watkinson [7]. Perhaps the most extreme form of saliency enhancement was used by Levinson [5], who simulated an intraoperative crisis of obvious importance to the well-being of the patient. The importance of measures to enhance the impact of the intraoperative material has been stressed by several investigators [6, 20], but positive results have been obtained also in studies in which no such measures have been taken [19]. It is, of course, possible that this omission contributed to our negative findings, and yet such a contention is essentially circular. To attribute a lack of memory for one set of verbal material (the test words) to the absence of another set of verbal material (a message stating its importance), which would itself require the anaesthetized subject to interpret and act upon it, is to assume in advance that verbal material can indeed be interpreted by the anaesthetized subject.

A wide variety of procedures has been used to attempt to establish memory for intraoperative verbal material, and no single type of test consistently gives positive results. Postoperative motor behaviour has been influenced by intraoperative verbal suggestion [6, 18, 20], but this procedure has been unsuccessful in patients in whom sentence completion did yield a positive result [21]. In some studies, a large battery of tests has been used and positive results have been obtained with some tests, although not with others; thus Block and others [19] found statistically significant recognition of nonsense words, but not of first names, played to the patient during anaesthesia.

No consistent anaesthetic regimen or anaesthetic depth has been associated with positive findings. Where the anaesthetic has been standardized, positive results have been obtained for sentence completion using a propofol infusion, but not with methohexitone infusion [21]. Likewise, positive results have been obtained with a word association test, using 0.5–1.5% isoflurane in oxygen, although not with 70% nitrous oxide supplemented by sufentanil [22].

In several of the studies in which the findings have indicated evidence of memory retention reaching statistical significance, the improvement in performance has been only modest. For example, preference for nonsense words played during anaesthesia reached a correct response rate of 56%, compared with 49% for control words—a difference reflecting about one correct word choice from the list of 16. Similarly, Bethune and others [21] obtained 15
correct responses from a possible total of 90 possible responses in a group of nine patients—a result which reached a high level of statistical significance, but which is of rather small magnitude.

Positive findings in this area would, if confirmed to be repeatable, be of considerable theoretical and practical importance. Studies obtaining negative results might conceivably have omitted an element necessary to the demonstration of memory preservation, but negative results cannot be artefactual; the occurrence of spuriously positive results reaching statistical significance is, however, bound to remain a danger. In the absence of a clearly emerging picture of the factors which allow memory preservation, positive results must be balanced against negative findings such as those in the present study.

REFERENCES