UNCONSCIOUS AUDITORY INFORMATION-PROCESSING DURING GENERAL ANAESTHESIA

UNCONSCIOUS AUDITORY INFORMATION-PROCESSING DURING GENERAL ANAESTHESIA

Onbewuste auditieve informatie-verwerking tijdens algehele anesthesie

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Erasmus Universiteit Rotterdam
op gezag van de Rector Magnificus
prof. dr. C.J. Rijnvos
en volgens besluit van het college van Dekanen.

de openbare verdediging zal plaatsvinden op
woensdag 30 september 1992 om 13.45 uur

door

Marko Jelicic

geboren te Amersham (GB.)

universiteits Erasmus DRUKKERIJ
1992

Promotie-commissie:

Promotor:	Prof. Dr. F. Verhage
Co-Promotor:	Dr. B. Bonke
Overige leden:	Prof. Dr. H. Collewijn
	Prof. K. Millar Ph.D.

To Marijke and Nick

CONTENTS

Chapter 1

Introduction: Hearing under anaesthesia?

A survey of preoperative fear in a large sample of surgical patients has shown that most patients worry about the anaesthesia they are going to have for their operations. These patients' greatest fears concern the possibility of not waking up after the operation, or of awakening during operation [1]. The fear of waking up while surgery is still in progress can be appreciated in the sense that about one per cent of all patients who have had surgical procedures under general anaesthesia have postoperative recollections of intraoperative events. Such recollections, primarily incidents of auditory perception, indicate "awareness" during general anaesthesia [2–4].

The introduction of balanced anaesthetic techniques involving the use of muscular blocking drugs seems to be responsible for the relatively high incidence of "awareness." Before the introduction of muscle relaxants in clinical anaesthesiology, some fifty years ago, anaesthetized patients breathed spontaneously and there was a generally well-recognized series of stages from light to deep anaesthesia [5]. In balanced anaesthesia respiratory pattern and eyeball movement are no longer available as signs of inadequate anaesthesia. Assessment of the state of anaesthesia is now carried out by monitoring the autonomic responses to surgery such as heart rate, blood pressure, pupil size, sweating and lacrimation. These parameters show considerable inter-individual variability and may be modified by drugs administered during anaesthesia (e.g., opioids, phenothiazines, adrenergic blockers and anticholinergics). Therefore, responses of autonomic activity are not always reliable indicators of the anaesthetic state, or detectors of "awareness" [6,7].

"Awareness during general anaesthesia" can lead to a variety of symptoms related to post-traumatic stress syndromes. About fifteen years ago, Blacher [8], a hospital psychiatrist and psychoanalyst, described six patients who had awakened from light anaesthesia while still unable to move. They sensed that something had gone terribly wrong and felt helpless. These patients suffered postoperatively from symptoms of anxiety and irritability, preoccupation with death, and repetitive nightmares. More recently, cases of psychological trauma after "awareness" experiences have been reported by Evans [9], Bennett [10], and by Moerman and Bonke [11].

Around 1960 the gyneacologist Cheek published case-studies which suggested that surgical patients had unconsciously registered sounds during adequate general anaesthesia [12-14]. He investigated a number of patients with a poor course of postoperative recovery. These women had no recall of intraoperative events. When hypnotized, however, they were allegedly able to recall "negatively coloured" statements that had been made about them, during surgery, by members of the surgical team.

Levinson [15,16], an anaesthesiologist who changed his specialty to psychiatry, described a female patient who had been involved in a serious motor car accident. She was having plastic surgery for facial injuries and had been referred to a psychiatrist to assist her in overcoming her fear of driving. Levinson used hypnosis in her therapy, and knew she was a good hypnotic subject. He decided to use one of her operations to examine the hypothesis that patients can unconsciously hear under anaesthesia. Levinson proposed to play music during surgery, and later in his office would hypnotize his patient and ask her what had been played during her surgical procedure. One aspect of the operation was the removal of a lump in her mouth. At a certain stage of the operation the experiment took an unexpected turn. The surgeon suddenly exclaimed that the lump was malignant. Somewhat later during the operation the lump proved to be a simple cyst. The anaesthesiologist had used thiopentone, nitrous oxide, oxygen and halothane for this procedure and was confident that the patient was adequately anaesthetized when the lump was removed. Postoperatively, the patient was extremely depressed, even though she knew the lump was non-malignant. One month after the surgical procedure she came to Levinson's office, and while hypnotized, she repeated the ominous words of the surgeon almost exactly.

Other patients with traumatic sequelae after unconscious perception of sounds during general anaesthesia have been reported by Goldmann and colleagues [17] and Howard [18]. It is possible that these cases of intraoperative stimulus registration are just the "tip of the iceberg," and some information-processing functions of the brain remain active during adequate anaesthesia.

This dissertation aims to examine the possibility of cognitive processing and memory storage in anaesthesia. It consists of four parts. The first section provides a brief outline of unconscious mental processes in psychological research. Next, a review of the experimental studies of unconscious perception during anaesthesia is given. The third part contains four empirical investigations of stimulus registration in anaesthetized patients. Finally, the research findings are evaluated, and implications for clinical practice in anaesthesiology and suggestions for future research are presented.

References

1. Ramsay MAE. A survey of preoperative fear. *Anaesthesia* 1972; *27:* 396-402.

2. Hutchinson R. Awareness during surgery. A study of its incidence. *British Journal of Anaesthesia* 1961; *33:* 463-469.

3. Wilson SL, Vaughan RW, Stephen CR. Awareness, dreams, and hallucinations associated with general anesthesia. *Anesthesia and Analgesia* 1975; *54:* 609-616.

4. Flier FJ, Smorenburg JMJ, Ent CK van der, Bonke B, Rupreht J. Postnarkotische Erinnerungs-fähigkeit, Angst und Träume bei chirurgischen Patienten. Eine klinische Studie. [A clinical study of postanaesthetic recall, anxiety and dreams in surgical patients.] *Anaesthesist* 1986; *35:* 609-612.

5. Guedel AE. *Inhalational Anesthesia: A Fundamental Guide.* New York: MacMillan, 1937.

6. Sebel PS. Evaluation of anaesthetic depth. *British Journal of Hospital Medicine* 1987; *38:* 116-117, 120-121, 124.

8. Blacher RS. On awakening paralyzed during surgery. A syndrome of traumatic neurosis. *Journal of the American Medical Association* 1975; *234:* 67-68.

9. Evans JM. Patients' experiences of awareness during general anaesthesia. In: Rosen M, Lunn JN, eds. *Consciousness, Awareness and Pain in General Anaesthesia.* London: Butterworths, 1987: 184-192.

10. Bennett HL. Memory for trauma surgery: Trauma victims talk back. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 237-243.

11. Moerman N, Bonke B. Psychische gevolgen van "awareness" bij algehele anesthesie. [Psychological consequences of "awareness" under general anaesthesia.] *Nederlands Tijdschrift voor Geneeskunde* 1990; *134:* 2465-2467.

12. Cheek DB. Unconscious perception of meaningful sounds during surgical anesthesia as revealed in hypnosis. *American Journal of Clinical Hypnosis* 1959; *1:* 101-113.

13 Cheek DB. The meaning of continued hearing sense under general chemo-anesthesia: A progress report and report of a case. *American Journal of Clinical Hypnosis* 1966; *8:* 275-280.

14. Cheek DB, LeCron LM. *Clinical Hypnotherapy.* New York: Grune & Stratton, 1968.

15. Levinson BW. States of awareness under general anaesthesia. A case history. *Medical Proceedings (S-Afr)* 1965; 243-245.

16. Levinson BW. States of awareness during general anaesthesia. In: Lassner J, ed. *Hypnosis and Psychosomatic Medicine.* Berlin: Springer, 1967: 200-207.

17. Goldmann L, Shah MV, Hebden M. Memory of cardiac anaesthesia. Psychological sequelae in cardiac patients of intraoperative suggestion and operating room conversation. *Anaesthesia* 1987; *42:* 596-603.

18. Howard JF. Incidents of auditory perception during anaesthesia with traumatic sequelae. *Medical Journal of Australia* 1987; *146:* 44-46.

Chapter 2

Unconscious mental processes in psychological research

About one century ago, the great American psychologist and philosopher William James warned that "the unconscious is the sovereign means for believing whatever one likes in psychology and turning what might become a science into a tumbling ground for whimsies" (p.107) [1]. Since then, psychology has taken different positions on the issue of unconscious mental processes [2,3]. A school of psychology named Radical Behaviourism not only rejected the unconscious but also rid itself of consciousness (the very subject matter of psychology according to James). Psychoanalysis, on the other hand, continued to base itself on unconscious processes and motives. In the 1950s, psychology abandoned a behaviourist point of view, and subjective and conscious events gained renewed importance. As cognition and consciousness returned to psychological science, interest in unconscious processes gradually revived [4-8].

This chapter provides a concise overview of some of the areas in which the effects of unconscious processes on psychological functioning are studied. These areas of research were selected on subjective motives and include subliminal perception, internal processing algorithms and implicit memory.

Subliminal perception

Subliminal perception refers to the processing of stimuli too weak in intensity or too brief in duration to be identified consciously [9,10]. The first systematic investigations on subliminal perception were published in the 1950s. The positive results in these studies were often regarded as experimental artefacts—the product of inappropriate methodologies and measures of awareness [11,12]. Research into subliminal perception became somewhat unfashionable in the 1960s and 1970s, but increased in popularity during the past ten years [13]. The strongest evidence for perception without conscious awareness comes from studies of backward-masking and the mere exposure effect.

In backward-masking studies subjects are briefly presented with single words followed by a meaningless jumble of lines. The shorter the time between onset of the first stimulus and onset of the second one, the less the observer is able to tell what had been shown in the first display. The second stimulus is called a pattern mask because it interferes with the perception of the target stimulus by virtue of its pattern. Marcel [14,15] exposed subjects to either a word or a blank field followed by a pattern mask. After each trial the subject had to make one of three decisions: (a) was there anything before the mask or not? (b) given two words, which of them was more similar visually to what had been presented? (c) given two words, which was more similar in meaning to what had been presented? Exposure of the stimulus was gradually diminished by lowering the duration of presentation. Eventually the pre-mask period became extremely brief. When the subjects reached chance performance on the presence/absence judgment, they were all still guessing above chance on the other two decisions. Next, they all reached chance on the graphic similarity decision, but were still guessing above chance on the judgment of meaning. In the end, of course, the subjects reached chance on the decision of meaning. Interestingly, while all subjects were guessing correctly, they claimed that they had not seen anything! Marcel's findings have successfully been replicated by at least three other research groups [16-18].

Other substantial evidence for subliminal perception is derived from studies which employed Zajonc's [19] mere exposure effect. This effect refers to the phenomenon that repeated presentation of a previously unfamiliar stimulus tends to increase its attractiveness. Kunst-Wilson and Zajonc [20] exposed subjects to a series of very brief presentations of geometrical stimuli. In the testing phase, subjects were presented with pairs of geometrical shapes—a new shape and one from the exposed set—for a somewhat longer period and subsequently asked to either judge which of the two shapes they liked better (or preferred) or decide which had been shown previously. Overall recognition judgments were at chance levels, but preference judgments showed a significant preference for the previously exposed stimuli. The Kunst-Wilson and Zajonc effect has been replicated and extended by several investigators [21-23].

Internal processing algorithms

Studies of subliminal perception show that the cognitive system is probably capable of processing incomparably more information than people are consciously aware of. Lewicki and Hill [24,25] claimed that unconscious information-processing is not merely limited to "low level" processing in order to support and maintain conscious psychological activity (e.g., storage and retrieval of information). They argued that even the most elementary perceptual operations such as determining distances between objects in three-dimensional space involve complex inferential strategies and algorithms (processing rules) for problem solving that are beyond one's conscious control.

Lewicki [26] introduced the concept of an internal processing algorithm for unconscious acquisition of information about covariation between features and events. He explained that the word "internal" emphasizes the idea that such an processing algorithm is represented in a code not directly accessible to examination in conscious awareness. Internal processing algorithms can be compared with so-called compiled computer programmes, which are executed very rapidly, but once compiled cannot flexibly be modified in run-time. For example, after unconsciously learning to encode a certain combination of information as humorous, the respective processing algorithm will instantly detect such a combination and will trigger immediate behavioural reaction (laughter). Lewicki compared consciously controlled processing of information with an interpreted programme. Both have their source code easily accessible, and their execution can be flexibly controlled and modified. The execution, however, is considerably slower than unconsciously determined cognitive processing.

Evidence for internal processing algorithms comes from various sources. In an influential paper, Nisbett and Wilson [27] discussed a number of social psychological studies which demonstrate that subjects had no access to inferential strategies that were responsible for their judgments or decisions. Subjects' perceptions of what they based their judgments on, were only reflections of private theories about how they had been reasoning, rather than reflections of the actual process of inference. In one of the studies reviewed by Nisbett and Wilson, for example, subjects evaluated articles of clothing, and there was a very strong tendency to prefer articles located in the right-hand position. When asked whether position of an article might have influenced their choice "virtually all subjects denied it, usually with a worried glance at the interviewer suggesting that they felt either that they had misunderstood the question or were dealing with a madman" (p.244).

Nisbett and Wilson [27] made a strong point concerning the unconscious nature of inferential strategies that are responsible for social judgments and decisions, and subjects' general lack of access to their own mental processes influencing their behaviour. In addition, Lewicki conducted a number of studies suggesting that subjects are able to acquire processing rules not only without being able to articulate what they had learned, but even without being aware that they had even learned anything [28,29]. In one study, subjects were presented with photographs and short descriptions of six young women [29]. Three of them were long-haired, and they were depicted as being very kind; the others were short-haired and were described as very capable. The material was arranged in such a way that these covariations were not salient and thus not accessible to the subjects' conscious awareness. In the testing phase, subjects were exposed to photographs of other women (with either long or short hair) and asked whether, in their opinion, the person was kind or capable. Lewicki found a clear effect of the covariation in stimulus material on judgment: Long-haired individuals were, in most cases, considered kind, whereas those with short hair were regarded capable.

Implicit memory

Perception and information-processing outside conscious awareness can influence behaviour and (social) judgments. Stimuli that are unconsciously perceived may also be stored in long-term memory. Evidence for this notion is derived from neuropsychological studies with amnesic patients, experimental psychological research employing normal subjects, and psychopharmacological experiments.

Patients are classified as amnesic when some brain damage renders them seemingly incapable of retaining new information (anterograde amnesia), but leaves other cognitive functions relatively intact [30]. These patients, e.g., those suffering from Korsakoff's syndrome, generally fail to learn the names of their nurses and doctors even after numerous meetings.

About twenty years ago, it was believed that amnesic patients were incapable of transferring new information from intact short-term memory to a long-term store [31]. Amnesics usually demonstrated normal performance on short-term memory tasks, but performed poorly on those involving long-term memory. Round about 1970 this view of the amnesic syndrome began to change when Warrington and Weiskrantz [32,33] showed that amnesic patients had unconscious, indirect long-term memory for recently presented material. They presented four amnesic and six control patients with 16 words to remember and then assessed their retention on two different memory tests. Each word had two essential properties: (a) at least 10 other words in the dictionary began with the same three letters; (b) the selected word was never the most common completion of the word-stem. After a 10 min interval, the subjects were given three letter word-stems that corresponded with eight of the stimulus words. They were simply requested to complete each stem with the first word that came to mind. Furthermore, the patients were administered a list of 16 words containing the remaining eight stimulus words, and were asked to identify the stimulus words using a yes/no recognition technique. The order in which word-completion and recognition were tested was constant for each patient but alternated between patients. As expected, the control patients outperformed the amnesics on the recognition task. The critical finding, however, was that there were no differences in retention between amnesic patients and controls on the word-completion test. It was concluded that the amnesics' normal performance on the completion task was due to indirect, unconscious memories of the stimulus words.

The word-completion test is called an implicit memory task. Subjects are instructed to complete each word-stem by producing the first word that comes to mind. This task does not require any conscious, or deliberate, recollection of a previous learning episode; memory is revealed by a facilitation or change in task performance attributable to information acquired during a learning period. In contrast, tests of recall and recognition involve conscious, or deliberate, remembering in the sense that subjects have to attempt to recollect their experiences.

These tests are therefore labeled explicit memory tasks [34-36].

The findings of Warrington and Weiskrantz [32,33] have been replicated many times [37,38]. Preserved unconscious learning in amnesic patients on implicit memory tests has also been reported with other tasks than word-completion. Shimamura [39] reviewed the literature and identified eight such tests (e.g., lexical decision, homophone spelling, free association and word identification) showing generally comparable effects.

The dissociation between implicit and explicit memory is not restricted to patients with the amnesic syndrome. Differences in conscious and unconscious memory have also been demonstrated in normal subjects (who do not suffer from brain injury). Eich [40] used a dual-task auditory shadowing paradigm to investigate indirect memory for unattended events. He had subjects shadow a passage of text presented to one ear, while word pairs were simultaneously presented to the other (unattended) ear. The word pairs consisted of a homophone (e.g., FAIR/FARE) and a word that biased its less common interpretation (e.g., taxi-FARE). The homophones could not be recognized. Yet implicit memory retention, measured by determining the likelihood of producing the biased interpretation of the homophones in a spelling test, was clearly present.

Ingenious research into implicit memory in normals was conducted by Jacoby and colleagues [41,42]. Subjects were asked to read names of nonfamous people under conditions of either full or divided attention (i.e., while performing a demanding listening task). Subsequently, they were given a list containing the previously presented names, plus new famous and nonfamous names, and were asked to identify (a) which names were famous and (b) which names they recognized as belonging to the list that had been given in the first phase of the experiment. The subjects were told that names they could remember from the list, were nonfamous. In the full attention condition, old nonfamous names were recognized, and more readily rejected as nonfamous, than were new nonfamous names. However, old nonfamous names could not be recognized as being previously administered in the divided attention condition, and were more likely to be called famous than new nonfamous names. It seems that, regardless of the level of attention, old nonfamous names had gained in familiarity. Full attention allowed subjects to later remember the source of a name's familiarity and so correctly judge it to be nonfamous. However, in the divided attention group, subjects were unable to recognize the previously read words and falsely attributed fame to the old nonfamous names because of their familiarity. The studies of Jacoby and co-workers nicely demonstrate implicit memory in the absence of explicit recollection.

In addition to the studies of amnesic patients and normals under divided attention, research on drug-induced amnesia demonstrated that diazepam and scopolamine reduced performance on recall and recognition tests but had little effect on implicit memory retention [43-45].

Does implicit memory merely reflect the activation of old, pre-existing knowledge, or can entirely new memory structures be formed? This is one the central issues in implicit memory theory [34]. Graf and Schacter [46,47] have produced evidence of indirect memory for new associations in normal subjects. However, implicit memory for new associative information may not be characteristic of all amnesic patients. For example, severely amnesics show good implicit memory for materials such as SOUR-GRAPES and SMALL-POTATOES—which are based on familiar speech idioms—but not for recombinations of these idioms such as SOUR-POTATOES and SMALL-GRAPES [48]. Several investigators have therefore argued that implicit memory in amnesic patients depends on a process of automatic activation, where pre-existing representations in memory are temporarily made more accessible as a consequence of an item's appearance on a study list [49-50]. However, a number of studies have reported implicit memory for new associations in patients with the amnesic syndrome. For instance, Johnson, Kim and Risse [51] demonstrated that a group of Korsakoff patients showed a normal, enhanced preference for Korean tunes, which they heard recently, although their explicit memory for these fragments of ethnic music was much impaired. As these amnesics were American, they had probably not heard the tunes before. Furthermore, Cermak and colleagues [52] tested the post-encephalitic amnesic patient S.S. on a perceptual identification test with real and pseudo-words and found that S.S. showed a normal increase in identification speed with both previously presented words and pseudo-words. Other evidence for new associative material in amnesics comes from a study by Moscovitch, Winocur and McLachlan [53]. It has been shown that when normal subjects are required to read degraded unrelated words they become faster on subsequent presentations. Moscovitch and co-workers found that amnesic patients showed this enhancement to a normal degree, which ability must have depended on the new associations they had formed during the first reading.

Conclusions

It seems that both elementary (e.g., pattern recognition) and high-level (e.g., social) perceptual-cognitive functions can operate outside conscious awareness. In addition, research with implicit memory tests has shown that unconsciously acquired material is stored in long-term memory. Unconscious information-processing can therefore be regarded as one of the fundamental properties of the cognitive system. See also [54,55] for conceptual models of unconscious mental processes.

References

1. James W. *The Principles of Psychology.* Chicago: Encyclopeadia Britannica, 1952 (originally published 1890).

2. Neisser U. *Cognitive Psychology.* New York: Appleton-Century-Crofts, 1967.

3. Schultz D. *A History of Modern Psychology* (3rd ed.). New York: Academic Press, 1981.

4. Shevrin H, Dickman S. The psychological unconscious. A necessary assumption for all psychological theory? *American Psychologist* 1980; *35:* 421-434.

5. Bowers KS. Revisioning the unconscious. *Canadian Psychologist* 1987; *28:* 93-104.

6. Kihlstrom JF. The cognitive unconscious. *Science* 1987; *237:* 1445-1452.

7. Mandler G, Nakamura Y. Aspects of consciousness. *Personality and Social Psychology Bulletin* 1987; *13:* 299-313.

8. Horowitz M, ed. *Psychodynamics and Cognition.* Chicago: The University of Chicago Press, 1988.

9. Dixon NF. *Subliminal Perception: The Nature of a Controversy.* London: McGraw-Hill, 1971.

10. Dixon NF. *Preconscious Processing.* New York: Wiley, 1981.

11. Eriksen CW. Discrimination and learning without awareness: A methodological survey and evaluation. *Psychological Review* 1960; *67:* 279-300.

12. Bevan W. Subliminal stimulation: A pervasive problem for psychology. *Psychological Bulletin* 1964; *61:* 89-99.

13. Bornstein RF. Subliminal techniques as propaganda tools: Review and critique. *The Journal of Mind and Behavior* 1989; *10:* 231-262.

14. Marcel AJ. Unconscious reading: Experiments on people who do not know that they are reading. *Visible language* 1978; *12:* 391-404.

15. Marcel AJ. Conscious and unconscious perception: Experiments on visual masking and word recognition. *Cognitive Psychology* 1983; *15:* 197-237.

16. Fowler CA, Wolford G, Slade R, Tassinary L. Lexical access with and without awareness. *Journal of Experimental Psychology* (General) 1981; *110:* 341-362.

17. Balota DA. Automatic semantic activation and episodic memory encoding. *Journal of Verbal Learning and Verbal Behavior* 1983; *22:* 88-104.

18. Greenwald AG, Klinger MR, Liu TJ. Unconscious processing of dichoptically masked words. *Memory & Cognition* 1989; *17:* 35-47.

19. Zajonc RB. Attitudinal effects of mere exposure. *Journal of Personality and Social Psychology* 1968; Monograph *9:* 1-27.

20. Kunst-Wilson WR, Zajonc RB. Affective discrimination of stimuli that cannot be recognized. *Science* 1980; *207:* 557-558.

21. Seamon JG, Marsh RL, Brody N. Critical importance of exposure duration for affective discrimination of stimuli that are not recognized. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1984; *10:* 465-469.

22. Bonnano GA, Stilling NA. Preference, familiarity, and recognition after repeated brief exposures to random geometric shapes. *American Journal of Psychology* 1986; *99:* 403-415.

23. Mandler G, Nakamura Y, Van Zandt BJS. Nonspecific effects of exposure on stimuli that cannot be recognized. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1987; *13:* 646-648.

24. Lewicki P, Hill T. Unconscious processes as explanations of behavior in cognitive, personality, and social psychology. *Personality and Social Psychology Bulletin* 1987; *13:* 355-362.

25. Lewicki P, Hill T. On the status of nonconscious processes in human cognition: Comment on Reber. *Journal of Experimental Psychology* (General) 1989; *118:* 239-241.

26. Lewicki P. *Nonconscious Social Information Processing.* New York: Academic Press, 1986.

27. Nisbett RE, Wilson TD. Telling more than we can know: Verbal reports on mental processes. *Psychological Review* 1977; *84:* 231-259.

28. Lewicki P. Nonconscious biasing effects of single instances on subsequent judgments. *Journal of Personality and Social Psychology* 1985; *48:* 563-574.

29. Lewicki P. Processing about covariations that cannot be articulated. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1986; *12:* 135-146.

30. Hirst W. The amnesic syndrome: Descriptions and explanations. *Psychological Bulletin* 1982; *91:* 435-460.

31. Baddeley A, Warrington EK. Amnesia and the distinction between long- and short term memory. *Journal of Verbal Learning and Verbal Behavior* 1970; *9:* 176-189.

32. Warrington EK, Weiskrantz L. Amnesia: Consolidation or retrieval? *Nature* 1970; *228:* 628-630.

33. Warrington EK, Weiskrantz L. The effect of prior learning on subsequent retention in amnesic patients. *Neuropsychologia* 1974; *12:* 419-428.

34. Schacter DL. Implicit memory: History and current status. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1987; *13:* 501-518.

35. Richardson-Klavehn A, Bjork RA. Measures of memory. *Annual Review of Psychology* 1988; *39:* 475-543.

36. Roediger HL III. Implicit memory. Retention without remembering. *American Psychologist* 1990; *45:* 1043-1056.

37. Graf P, Squire LR, Mandler G. The information that amnesic patients do not forget. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1984; *10:* 164-178.

38. Squire LR, Shimamura AP, Graf P. Independence of recognition memory and priming effects: A neuropsychological analysis. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1985; *11:* 37-44.

39. Shimamura AP. Priming effects in amnesia: Evidence for a dissociable memory function. Quarterly *Journal of Experimental Psychology* 1986; *38A:* 619-644.

40. Eich E. Memory for unattended events: Remembering with and without awareness. *Memory & Cognition* 1984; *12:* 105-111.

41. Jacoby LL, Kelley CM. Unconscious influences of memory for a prior event. *Personality and Social Psychology Bulletin* 1987; *13:* 314-336.

42. Jacoby LL, Woloshyn V, Kelley CM. Becoming famous without being recognized: Unconscious influences of memory produced by dividing attention. *Journal of Experimental Psychology* (General) 1989; *118:* 115-125.

43. Fang JC, Hinrichs JV, Ghoneim MM. Diazepam and memory: Evidence for spared memory function. *Pharmacology Biochemistry & Behavior* 1987; *28:* 347-352.

44. Danion JM, Zimmerman MA, Willard-Schroeder D, Grangé D, Singer L. Diazepam induces a dissociation between explicit and implicit memory. *Psychopharmacology* 1989; *99:* 238-243.

45. Nissen MJ, Knopman DS, Schacter DL. Neurochemical dissociation of memory systems. *Neurology* 1987; *37:* 789-794.

46. Graf P, Schacter Dl. Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1985; *11:* 501-518.

47. Schacter DL, Graf P. Effects of elaborative processing on implicit memory for new associations. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1986; *12:* 432-444.

48. Schacter DL, Graf P. Preserved learning in amnesic patients: Perspectives from research on direct priming. *Journal of Clinical and Experimental Neuropsychology* 1986; *8:* 727-743.

49. Warrington EK, Weiskrantz L. Amnesia: A disconnection syndrome? *Neuropsychologia* 1982; *20:* 233-248.

50. Diamond R, Rozin P. Activation of existing memories in anterograde amnesia. *Journal of Abnormal Psychology* 1984; *93:* 98-105.

51. Johnson MK, Kim JK, Risse G. Do alcoholic Korsakoff's syndrome patients acquire affective reactions? *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1985; *11:* 27-36.

52. Cermak LS, Blackford SP, O'Connor M, Bleich RP. The implicit memory ability of a patient with amnesia due to encephalitis. *Brain and Cognition* 1988; *7:* 145-156.

53. Moscovitch M, Winocur G, McLachlan D. Memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology* (General) 1986; *115:* 331-347.

54. Marcel AJ. Conscious and unconscious perception: An approach to the relations between phenomenal experience and perceptual processes. *Cognitive Psychology* 1983; *15:* 238-300.

55. Kihlstrom JF. Conscious, subconscious, unconscious: A cognitive perspective. In: Bowers KS, Meichenbaum D, eds. *The Unconscious Reconsidered.* New York: Wiley, 1984: 149-211.

Chapter 3

Unconscious information-processing during general anaesthesia: Review of the experimental literature

The case-studies which suggested unconscious perception of sounds during general anaesthesia some 30 years ago (see Chapter 1), resulted in attempts to demonstrate such perception by experimental means. In 1977, Trustman, Dubovsky and Titley [1] reviewed seven experimental studies of cognitive processing in anaesthetized patients. They concluded that all seven had methodological problems. Some investigators had failed to apply a double-blind procedure, making their research vulnerable to demand characteristics and experimenter effects. Furthermore, a number of studies lacked baseline testing conditions or untreated control groups that would permit valid inferences about what had occurred during surgery. Trustman and colleagues therefore offered useful suggestions for properly conducting future research projects into stimulus registration during anaesthesia.

Since the Trustman and co-workers review [1], many studies of unconscious information-processing under anaesthesia have been published. At present, this field of research is attracting more attention than ever before. Anaesthesiologists have recognized the potential danger of stimulus registration during anaesthesia and have started to investigate auditory evoked potentials in the electro-encephalogram (E.E.G.) of anaesthetized patients [2-4]. Experimental psychologists, on the other hand, have searched for research problems outside the "artificial" laboratory situation and have used paradigms from cognitive psychology (see Chapter 2) to study perception during anaesthesia [5-7]. A few years ago, the first book on this topic "Consciousness, Awareness and Pain in General Anaesthesia" [8] was published, and in April 1989 the "First International Symposium on Memory and Awareness in Anaesthesia" was held in Glasgow (Scotland). The proceedings of this symposium were subsequently published in 1990 as "Memory and Awareness in Anaesthesia" [9]. The second international symposium was held April 1992 in Atlanta (U.S.A.).

Although several excellent reviews of the literature have been published [10-12] developments in this area of research are going quite fast, so that an up-to-date account of the empirical findings seems in order. Therefore, this chapter provides a "state of the art" review of the experimental literature on cognitive processing under general anaesthesia. Four research-strategies are discussed.

Hypnosis

One of the first studies on stimulus registration during anaesthesia was carried out by Levinson [13,14]. Ten volunteer patients who had general anaesthesia for minor surgery were subjected to a mock crisis, in which the anaesthesiologist had the operation stopped by stating that the patient had turned blue and needed oxygen. One month later the patients were hypnotized and age-regressed to the time of surgery. Four of them were able to repeat almost exactly the words of the anaesthesiologist. Another four remembered having heard something, and some of them were able to identify the speaker as the anaesthesiologist. The latter group all showed marked anxiety. None had any conscious recall of intraoperative events.

It is difficult to evaluate the validity of this highly unethical experiment, because the hypnotist (Levinson) knew what had occurred during the experimental situation and might thus have been able to influence the patients' behaviour under hypnosis. On the other hand, if this has been the case, it remains to be answered why the patients' reactions were so outspoken.

Postoperative motor responses

Other researchers have investigated information-processing in anaesthetized patients through intraoperative suggestions to touch a specific body part during a visit of the experimenter after the operation.

Bennett, Davis and Giannini [15] randomly assigned 33 surgical patients to two groups. In the experimental condition, 11 patients received, while under anaesthesia, suggestions to pull an ear during the postoperative interview. The control group, consisting of 22 patients, were given no suggestions. None of the patients had any conscious recall of intraoperative events, but data-analysis "showed" that experimental patients pulled their ears more frequently, and longer, than controls.

Thirty patients undergoing cardiac surgery were allocated, at random, to two groups in a replication study by Goldmann, Shah and Hebden [16]. Twenty-one of them were presented with intraoperative suggestions to touch their chin during the investigators' ward round. The other nine did not receive any suggestions. Goldmann and co-workers reported that patients who had been administered suggestions, touched their chins more often than those who had not heard intraoperative messages. Three patients had conscious recollections of events occurring during surgery.

The above two investigations raised a number of criticisms [11,17]. First, the suggestions were presented towards the end of surgery when the anaesthetic state might have been allowed to lighten. The intraoperative messages may therefore have been perceived in a semiconscious state. Second, no base-line "ear-pulling" or "chin-touching" assessment was taken prior to giving the postoperative motor suggestion. Without this base-line level, one cannot determine whether the postoperative differences between the groups were due to the intraoperative suggestion or to chance allocation of patients to groups. With such small sample sizes, and the biased allocation to conditions, the latter probability is high. Third, close inspection of the data reveals that the differences between experimental and control groups are due to extreme reactions of only a few patients (two in the Bennett et al. study and four in the Goldmann et al. experiment).

Block, Ghoneim, Sum Ping and Ali [18] presented 72 anaesthetized patients with suggestions to touch a particular body part in a randomized study. Half the patients were instructed to pull an ear, the other half to touch the nose. During the postoperative interview, patients touched the "correct" (suggested) part of the body longer than the "incorrect" (not suggested) body part. None of the patients reported any recall of intraoperative events.

Two experiments did not find an effect of postoperative motor suggestions. In a study by McLintock, Aitken, Downie and Kenny [19] 40 patients scheduled for hysterectomy were randomly assigned to an experimental and a control group. Under anaesthesia, half the patients were requested to touch their ear during the postoperative interview. The other patients were not played suggestions. No differences in suggested motor responses were found between the two groups.

Jansen, Bonke, Klein, van Dasselaar and Hop [20] used a more sophisticated methodology to study stimulus registration in anaesthetized patients. Eighty surgical patients were allocated, at random, to a suggestion or a control group. Preoperatively, a baseline assessment was made to establish the patients' natural frequency of ear-pulling behaviour. During surgery, 38 patients received instructions to touch an ear during a postoperative ward round. The other patients were not given suggestions. Experimental patients did not pull their ear more often than controls.

Studies in which patients are suggested, during surgery, to demonstrate a specific motor response, hardly produce any convincing evidence for cognitive processing during general anaesthesia. Two of the five investigations reviewed here, yielded negative effects, and in addition, two of the three with positive results are methodologically flawed.

Therapeutic suggestions

Some investigators have used therapeutic suggestions to study stimulus registration in anaesthetized patients. They hypothesized that, since inappropriate or misinterpreted remarks might have a harmful effect on recovery after surgery, statements suggesting a quick and uncomplicated course, administered during anaesthesia, would possibly have a beneficial effect on postoperative course.

Three studies, which were published around 1960, reported a positive effect of therapeutic suggestions, presented during anaesthesia, on postoperative well-being. However, these early investigations had substantial methodological problems (e.g., absence of control group and/or lack of double-blind procedure) [1].

About twenty years later, Bonke, Schmitz, Verhage and Zwaveling [21] conducted an experiment without methodological shortcomings. They randomly assigned 91 patients undergoing biliary tract surgery to one of three groups. During anaesthesia, 31 of them received therapeutic suggestions, such as "You are completely relaxed. . .after the operation you will feel fine and comfortable, and you will heal quickly" and "Great. . .that looks excellent. . .This patient will soon be cured and able to go home." The others, two groups of 30 patients, were intraoperatively exposed to white noise or actual operating theatre sounds. None of the patients reported any recall of the administered sounds. However, data-analysis revealed that patients older than 55 years who had been played positive messages left the hospital sooner than those presented with other sounds. Therefore, Bonke and colleagues argued that therapeutic suggestions protected older patients against prolonged postoperative stay in hospital.

In an investigation by Evans and Richardson [22], 39 hysterectomy patients were allocated, at random, to two groups. In the experimental condition, 19 patients were given therapeutic messages during anaesthesia. The other patients did not receive any suggestions. Evans and Richardson found that patients having been exposed to positive suggestions spent less time in hospital, suffered a shorter period of pyrexia, and were generally rated a better than expected recovery by the nursing staff than control patients. Again, there were no patients with explicit recollections of events occurring during surgery.

Münch and Zug [23] randomly, and evenly, assigned 36 patients scheduled for thyroidectomy to an experimental and a control group. Under anaesthesia, experimental patients were presented with therapeutic suggestions, while controls were not exposed to any intraoperative messages. Patients in the suggestion group reported a more favourable postoperative subjective well-being than those in the control condition. None of the patients recalled any intraoperative event.

Sixty hysterectomy patients were allocated to two groups, in a randomized experiment by McLintock, Aitken, Downie and Kenny [24]. While anaesthetized, 30 of them received therapeutic messages. The remaining patients were not exposed to suggestions. McLintock and co-workers used patient-controlled analgesia and tested the amount of postoperative pain medication. Patients in the experimental condition had a lower morphine consumption in the postoperative phase than control patients. There were no patients with recall of events that had taken place during the surgical procedure.

In addition to the four properly conducted investigations described above, two other recent studies produced "evidence" for improved and accelerated recovery after intra-anaesthetic positive suggestions [25,26]. However, these experiments did not control for type of surgery. It is therefore possible that the favourable postoperative course in experimental patients was due to a lower number of major surgical procedures as compared with the controls.

Wood, Gibson and Longo [27] found a trend for improved well-being after therapeutic suggestions, presented during anaesthesia. They randomly assigned 67 children undergoing tonsillectomy and adenoidectomy to one of three groups. Thirty-one patients in the experimental and 19 patients in the placebo condition received positive suggestions recited in English and French respectively. Seventeen other patients did not receive any therapeutic messages. A composite measure of seven outcome variables revealed that patients who had been exposed to English suggestions demonstrated a more favourable postoperative course than patients in the placebo and control groups. These differences were nonetheless not statistically significant. Patients with the highest risk for poor recovery (i.e., those with a poor preoperative status) benefited most from the English suggestions. None of the children was able to recall intraoperative events.

One hundred and six cholecystectomy patients were divided, at random, into four groups in a study by Boeke, Bonke, Bouwhuis-Hoogerwerf, Bovill and Zwaveling [28]. During anaesthesia, 24 of them were presented with therapeutic messages. Twenty-six others received nonsense suggestions and 27 seaside sounds. The remaining 29 patients were exposed to actual operating theatre sounds. Although Boeke and co-workers failed to find statistically significant differences between the four groups in postoperative course, close inspection of their data shows that patients who had been played positive suggestions reported a somewhat more favourable subjective well-being than those exposed to other sounds. There were no patients with explicit memories of events occurring during surgery.

Woo, Seltzer and Marr [29] reported no effect of therapeutic suggestions, given during anaesthesia, on postoperative recovery in hysterectomy patients. However, this study was criticized on methodological grounds (i.e., small sample size) [30].

Block, Ghoneim, Sum Ping and Ali [31] studied 209 patients undergoing six types of surgical procedures in a randomized (and matched) study. During anaesthesia, 109 of them were played a recording predicting a smooth recovery and a postoperative stay without pain, nausea or vomiting. The other 100 patients were exposed to a blank tape. Block and co-workers found no differences in postoperative recovery between the two groups.

Seventy-three hysterectomy patients were randomly allocated to one of three groups, in an experiment by Liu, Standen and Aitkenhead [32]. While anaesthetized, 24 patients were administered positive suggestions, 25 others received a modified history of the hospital in which the operation took place, and the remaining 24 patients were exposed to blank recordings with no messages. Liu and colleagues were unable to show a more favourable course after intraoperative therapeutic suggestions.

Studies which employed positive suggestions during surgery, provide evidence of unconscious perception of sounds in anaesthetized patients. Improved recovery and/or reduced postoperative stay in hospital after intraoperative suggestions has been reported in four of the eight properly conducted investigations. Two other experiments yielded a trend towards a more favourable well-being after therapeutic messages. The investigations by Block and colleagues [31] and Liu and co-workers [32] were the only studies without methodological problems, in which no effect of therapeutic suggestions could be demonstrated.

Implicit memory tests

Implicit memory tests (see Chapter 2) have recently been used to investigate unconscious information-processing during anaesthesia. Wolters and Phaf [33] hypothesized that the learning mechanisms involved in implicit and explicit memory retention are different: explicit learning requires attention at time of encoding, whereas implicit, or unconscious learning seems to be an automatic process not dependent upon energetic, or attentional, processing. Anaesthetized patients are, by definition, unable to attend to information, and therefore to recall stimuli presented during surgery. Since implicit learning does not involve attentional processing, they may yet demonstrate implicit memory for events occurring during anaesthesia.

Millar and Watkinson [34] allocated 53 surgical patients, at random, to experimental or control groups. Twenty-seven of them were administered a list of ten target words during anaesthesia. The other patients were played a tape of radio static. In the postoperative phase, all patients were presented with a list of 40 words, containing the target words, and were asked to designate which words they had heard under anaesthesia. None of the patients had any conscious recollection of intraoperative events. However, experimental patients were better able than controls to discriminate between target and non-target words, suggesting that they had preserved some weak, implicit memory of the stimulus list.

Nineteen patients were randomly assigned to two groups by Goldmann [35]. Prior to surgery all patients were given a "general knowledge" questionnaire. This multiple choice test consisted of 16 questions, ten of which were obscure (e.g., What is the blood pressure of an octopus?). Under anaesthesia, nine patients received the correct answers to the obscure items of the questionnaire (e.g., The blood pressure of an octopus is 70 mg of mercury). The control patients did not receive any intraoperative messages. After the surgical procedure, the "general knowledge" test was administered anew. Goldmann reported that there was no difference between the two groups with respect to preoperative scores on the knowledge test. Postoperatively, however, experimental patients correctly answered more questions about obscure facts than controls. Thus, patients in the experimental condition demonstrated implicit memory for the obscure facts. There were no patients with explicit recollections of intraoperative events.

Roorda-Hrdličková, Wolters, Bonke and Phaf [36] allocated 81 patients, at random, to an experimental and a control condition. While anaesthetized, 43 of them were presented with two target words from each of two semantic categories. These target words were familiar, but not the most frequently used words from the two categories. The other patients were played neutral sounds. After the operation, none of the patients was able to remember having heard anything during surgery. When asked to name the first three exemplars of the two experimental categories that came to mind, however, the experimental patients generated almost three times as many target words as patients in the control group.

Twenty-four surgical patients were studied by Humphreys, Asbury and Millar [37]. During feedback controlled anaesthesia, patients were administered—depending upon the end-tidal (ET) concentration of isoflurane—one of two tapes, each containing a list of ten homophones (e.g., HERE/HEAR) accompanied with a few words that biased, or primed, the homophones toward their less common use (e.g., HERE and there). Tape A was played when the ET isoflurane concentration was $\leqslant 1.2$ per cent, tape B when it was > 1.2 per cent. In the postoperative phase, patients received a list of 40 homophones, containing the homophones from tapes A and B, and were asked to free-associate to the homophones (i.e., say the first thing that came into their heads). Although they found no overall effect, Humphreys and colleagues found more priming of homophones from tape A (ET isoflurane $\leqslant 1.2$ %) than from tape B (ET isoflurane > 1.2 %). None of the patients reported any explicit memories of events that had taken place during surgery.

Kihlstrom, Schacter, Cork, Hurt and Behr [38] presented paired associates to 25 anaesthetized patients in a double-blind study. After the surgical procedure, all patients were given tests of cued recall and recognition to assess explicit memory performance, and a free-association test to measure implicit memory retention. There were no patients with explicit recollections of the paired associates presented during anaesthesia, but a majority of them demonstrated a small priming effect on the word-association test.

Seventy-two patients were administered lists of words and nonsense words during anaesthesia in an study by Block, Ghoneim, Sum Ping and Ali [18]. Postoperatively, they were given two implicit memory tests to determine verbal learning during surgery. In a word-completion test, patients who were shown a page containing the first three letters of words and asked to give words beginning with those letters, mentioned more words from the list that had been played during anaesthesia than from a list not played. In a nonsense words test, patients who were presented different nonsense words intraoperatively, preferred and guessed more accurately the words that had been presented most often, relative to those presented less often. None of the patients were able to remember anything of the word lists played under anaesthesia.

Three experiments did not yield evidence of implicit memory for stimuli presented during anaesthesia. Eich, Reeves and Katz [39] randomly assigned 48 patients to two groups. Prior to surgery, 24 patients were administered a list of 12 homophones that were biased toward their less common interpretation. The others received the homophones while anaesthetized. Postoperatively, the patients were given a list of 48 homophones containing the 12 experimental ones, and were given tests of recognition and spelling. None of the patients who were played the list of homophones during surgery, recognized the experimental homophones or spelled them according to their less common interpretation. Unfortunately, the methodology of this study was less than optimal. First, Eich and co-workers presented the biased homophones only once, and just for a short period. Probably, auditory stimuli have to be presented at least a number of times during anaesthesia before an implicit memory effect can be found. Second, patients were not prevented from picking up possibly interfering words or phrases before and after stimulus presentation. Third, postoperative testing for implicit memory did not take place before the fourth or fifth day after surgery. Such a long retention interval may have led to the disappearance of an effect.

The "mere exposure" paradigm was used in a double-blind study by Winograd, Sebel, Goldman and Clifton [40] (see Chapter 2 for a description of the mere exposure effect). Twenty anaesthetized patients were zero, three or twelve times exposed to fragments of traditional instrumental ethnic music. After the operation, patients were again played the tunes and were asked to give a preference rating. Winograd and colleagues did not find a relationship between number of intraoperative exposures and implicit, preference ratings. However, Millar [11] points out that a "preference" study might not be appropriate in the context of anaesthesia and surgery. Given the inevitable anxiety and discomfort associated with surgical procedures, it would be surprising if patients showed a preference for music associated with such trauma.

Bonke, Van Dam, Van Kleef and Slijper [41] randomly allocated 80 pediatric surgical patients to two groups. During anaesthesia, 40 of them were played neutral phrases which included the colour Orange. The other 40 patients were presented with phrases including the colour Green. A pilot study of colour preference in children had shown that orange and green were not the most favourite, but still well-known, colours. About one day after the operation, the patients were given a colouring task to detect preference for the colour named under anaesthesia. Bonke and his colleagues were unable to demonstrate implicit memory for the colours administered during surgery. There are, however, a few problems associated with this investigation. As argued above, a "preference" study might not be useful in the context of stressful medical procedures. Second, it is possible that young children lack a stable memory representation. Third, the long delay between presentation and testing might have obscured an implicit memory effect. In other studies positive findings were generally found with relatively short delays.

Investigations which used implicit memory tests provide convincing evidence for cognitive processing during general anaesthesia. Seven properly conducted experiments produced positive effects, while, on the other hand, three experiments that yielded null effects all had methodological problems.

Discussion

What is the status of unconscious perception of sounds during general anaesthesia, some 15 years after the Trustman, Dubovsky and Titley [1] review?

Apparently, a number of researchers were not aware of the recommendations put forward by Trustman and colleagues: some recent studies of information-processing under anaesthesia suffer from inadequate methodologies, poor control or statistical difficulties. But what can be inferred from the properly conducted investigations? In contrast with experiments employing therapeutic suggestions or implicit memory tests, studies which used postoperative motor responses have not produced evidence of stimulus registration under anaesthesia. Patients' motivation and personality traits as "absorption" and "openness to experience" are likely to be involved in responding to suggestions to touch a specific body part after the operation [12]. It might, for that reason, be difficult to elicit postoperative motor responses during surgery.

Unconscious perception during anaesthesia has been demonstrated in most "therapeutic suggestions" studies. Patients who had been administered positive suggestions showed, in general, a more favourable postoperative course than those exposed to neutral sounds. However, there is considerable variation in the effect of therapeutic messages on recovery after surgery. A number of studies found a small effect, or none whatsoever, of suggestions, whereas other investigations yielded large effects. The widely used subjective measurements of well-being and parameters recorded by the medical staff are perhaps somewhat too insensitive to detect influences of suggestions on postoperative recovery [11]. It is also possible that some therapeutic suggestions have a greater impact on postoperative course than others [42].

Studies which used implicit memory tests provide the most convincing evidence of stimulus registration in anaesthetized patients. Virtually all experiments show a facilitation or change in task performance attributable to stimuli presented during anaesthesia. However, nearly all investigations have involved the activation of pre-existing knowledge in postoperative indirect memory. Therefore, it remains unclear whether or not new verbal associations can be formed in implicit memory whilst under anaesthesia.

One underlying assumption of the experiments reviewed in this chapter, is that the patients had been "adequately" anaesthetized at the time of administration of experimental stimuli. Most authors report that none of their patients had conscious recollection of intraoperative events. This, however, does not automatically imply that the experimental sounds were perceived during a steady state of anaesthesia. Russell [43], for instance, described patients who had been able to respond to verbal commands during anaesthesia, but were nevertheless completely amnesic for events that had occurred during surgery. Therefore, in the studies with positive results, there may have been a slight chance that cognitive processing took place because information was presented simultaneously with a brief lightening in the state of anaesthesia. This remote possibility of information-processing during temporarily lightened stages of anaesthesia has no consequences for the external validity of the experiments discussed here.

The anaesthetic techniques and procedures in these investigations were very much the same as those used in clinical practice. The reviewed studies tell us something about the occurrence of unconscious perception during normal, routine clinical anaesthesia.

Conclusions

Most of the experiments without methodological problems, in this review, demonstrate stimulus registration in anaesthetized patients. Cognitive processing and memory storage under anaesthesia can therefore be considered real phenomena. Additional support for this notion comes from neurophysiological investigations. Studies which employed evoked responses in the E.E.G. have shown that auditory signals are transmitted to the cerebral cortex under clinical doses of anaesthetics [2-4]. At the moment, however, little is known about the factors that influence unconscious perception of sounds during anaesthesia. Particular anaesthetic cocktails, premedicant drugs, stimulus features and patient characteristics may all affect information-processing under general anaesthesia.

References

1. Trustman R, Dubovsky S, Titley R. Auditory perception during general anesthesia—myth or fact? *The International Journal of Clinical and Experimental Hypnosis* 1977; *25:* 88-105.

2. Jones JG, Thornton C, Heneghan CPH, James MFM, Navaratnarajan M. The use of the auditory evoked response to measure graded effects of general anaesthetics. In: Beneken JEW, Lavelle SM, eds. *Objective Medical Decision-Making; Systems Approach in Acute Disease.* Berlin: Springer, 1983: 57-64.

3. Sebel PS, Heneghan CP, Ingram DA. Evoked responses—a neurophysiological indicator of depth of anaesthesia? *British Journal of Anaesthesia* 1985; *57:* 841-842.

4. Jones JG, Konieczko K. Hearing and memory in anaesthetised patients. *British Medical Journal* 1986; *292:* 1291-1293.

5. Millar K. Assessment of memory for anaesthesia. In: Hindmarch I,Jones JG, Moss E, eds. *Aspects of Recovery from Anaesthesia.* London:Wiley, 1987: 75-91.

6. Goldmann L. Further evidence for cognitive processing under general anaesthesia. In: Rosen M, Lunn JN, eds. *Consciousness, Awareness and Pain in General Anaesthesia.* London: Butterworths, 1987: 140-144.

7. Bennett HL. Perception and memory for events during adequate general anesthesia for surgical operations. In: Pettinati H, ed. *Hypnosis and Memory.* New York: Guilford Press, 1988: 193-231.

8. Rosen M, Lunn JN, eds. *Consciousness, Awareness and Pain in General Anaesthesia.* London: Butterworths, 1988.

9. Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990.

10. Goldmann L. Information-processing under general anaesthesia: A review. *Journal of the Royal Society of Medicine* 1988; *81:* 224-227.

11. Millar K. Recall, recognition and implicit memory for intra-anaesthetic events. *Baillière's Clinical Anaesthesiology* 1989; *3:* 487-510.

12. Kihlstrom JF, Schacter DL. Anaesthesia, amnesia, and the cognitive unconscious. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 21-44.

13. Levinson BW. States of awareness during general anaesthesia. *British Journal of Anaesthesia* 1965; *37:* 544-546.

14. Levinson BW. The states of awareness in anaesthesia in 1965. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 11-18.

15. Bennett HL, Davis HS, Giannini JA. Non-verbal response to intraoperative conversation. *British Journal of Anaesthesia* 1985; *57:* 174-179.

16. Goldmann L, Shah MV, Hebden M. Memory of cardiac anaesthesia. Psychological sequelae in cardiac patients of intraoperative suggestion and operating room conversation. *Anaesthesia* 1987; *42:* 596-603.

17. Millar K. Unconscious perception during anaesthesia (letter). *British Journal of Anaesthesia* 1987; *59:* 1334-1335.

18. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Human learning during general anaesthesia and surgery. *British Journal of Anaesthesia* 1991; *66:* 170-178.

19. McLintock TTC, Aitken H, Downie C, Kenny GNC. The effect of intraoperative suggestions on postoperative analgesic requirements. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 96-100.

20. Jansen CK, Bonke B, Klein J, Van Dasselaar N, Hop WCJ. Failure to demonstrate unconscious perception during balanced anaesthesia by postoperative motor response. *Acta Anaesthesiologica Scandinavica* 1991; *35:* 407-410.

21. Bonke B, Schmitz PIM, Verhage F, Zwaveling A. Clinical study of so-called unconscious perception during general anaesthesia. *British Journal of Anaesthesia* 1986; *58:* 957-964.

22. Evans C, Richardson PH. Improved recovery and reduced postoperative stay after therapeutic suggestions during general anaesthesia. *Lancet* 1988; *ii:* 491-493.

23. Münch F, Zug HD. Do intraoperative suggestions prevent nausea and vomiting in thyroidectomy-patients? An experimental study. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 185-188.

24. McLintock TTC, Aitken H, Downie CFA, Kenny GNC. Postoperative analgesic requirements in patients exposed to positive intraoperative suggestions. *British Medical Journal* 1990; *301:* 788-790.

25. Rath BW. *The Use of Suggestions during General Anesthesia.* Ph.D. dissertation. University of Louisville, 1982

26. Furlong M. Positive suggestions presented during anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 170-175.

27. Wood WE, Gibson W, Longo D. Moderation of morbidity following tonsillectomy and adenoidectomy: a study of awareness under anesthesia. International *Journal of Pediatric Otorhinolaryngology* 1990; *20:* 93-105.

28. Boeke S, Bonke B, Bouwhuis-Hoogerwerf ML, Bovill JG, Zwaveling A. Effects of sounds presented during general anaesthesia on postoperative course. *British Journal of Anaesthesia* 1988; *60:* 697-702.

29. Woo R, Seltzer JL, Marr A. The lack of response to suggestion under controlled surgical anaesthesia. *Acta Anaesthesiologica Scandinavica* 1987; *31:* 567-571.

30. Bonke B, Jelicic M, Strik R van. Comment on Woo, Seltzer and Marr. *Acta Anaesthesiologica Scandinavica* 1988; *32:* 712-713.

31. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Efficacy of therapeutic suggestions for improved postoperative recovery presented during general anesthesia. *Anesthesiology* 1991; *75:* 746-755.

32. Liu WHD, Standen P, Aitkenhead AR. Therapeutic suggestions during general anaesthesia in patients undergoing hysterectomy. *British Journal of Anaesthesia* 1992; *68:* 277-281.

33. Wolters G, Phaf RH. Explicit and implicit measures of memory: Evidence for two learning mechanisms. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 57-63.

34. Millar K, Watkinson N. Recognition of words presented during general anaesthesia. *Ergonomics* 1983; *26:* 585-594.

35. Goldmann, L. *Awareness under General Anaesthesia.* Ph.D. dissertation. University of Cambridge, 1986.

36. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 150-155.

37. Humphreys KJ, Asbury AJ, Millar K. Investigation of awareness by homophone priming during computer controlled anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 101-109.

38. Kihlstrom JF, Schacter DL, Cork RC, Hurt A, Behr SE. Implicit and explicit memory following surgical anesthesia. *Psychological Science* 1990; *1:* 303-306.

39. Eich E, Reeves JL, Katz RL. Anesthesia, amnesia, and the memory/awareness distinction. *Anesthesia and Analgesia* 1985; *64:* 1143-1148.

40. Winograd E, Sebel PS, Goldman WP, Clifton CL. Indirect assessment of memory for music under anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 181-184.

41. Bonke B, Van Dam ME, Van Kleef JW, Slijper FME. Implicit memory tested in children with inhalation anaesthesia. *Anaesthesia,* in press.

42. Bonke B. Psychological consequences of so-called unconscious perception and awareness in anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 197-218.

43. Russell IF. The isolated forearm technique. Relationship between movements and clinical indices. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 316-319.

Chapter 4

Line of research

In the previous chapter (Chapter 3), a review of the experimental literature on unconscious perception of sounds during anaesthesia was given. It was concluded that some amount of information-processing takes place in anaesthetized patients, but little is yet known about the exact nature of such stimulus registration (see also Kihlstrom and Schacter [1]). In pursuing cognitive processing under anaesthesia, two research strategies seem useful.

Studies which used intraoperative positive suggestions have provided evidence of unconscious perception during anaesthesia. Patients who had been exposed to therapeutic messages, whilst under anaesthesia, showed a more favourable postoperative recovery than controls. However, there is remarkable variation in response to suggestions. Some researchers found a small or no effect of therapeutic messages, whereas others reported a large effect. Differences in grammatical structure of the employed suggestions may account for this discrepancy. When faced with the threat of impending surgery and anaesthesia, many patients will get anxious. This anxiety, which does not necessarily present itself as such, may trigger off a psychological regression back to previous phases in the development of human functioning [2]. Anxiety-induced regression makes an individual fall back to previously used methods of dealing with problems, threats and conflicts. Very often these methods date back to early childhood in which the infant can feel itself protected by the ever-present mother. The way of thinking, in particular, can easily regress to a "primitive" mode, i.e., from abstract to concrete, from "secondary-process thinking" to "primary-process thinking" [3]. In this "primitive" mode of thinking everything is absolute; there are no linguistic nuances, nor is there any room for cause and effect relations, logic, or reality testing. It is therefore not unlikely that affirmative positive suggestions (e.g., "You will feel fine after the operation"), presented under anaesthesia, but not grammatical negatives (e.g., "You will *not* feel nauseous; you will *not* have any pain") have a beneficial effect on postoperative well-being. Chapter 5 describes an experiment designed to investigate the "essential ingredients" of therapeutic messages, presented during anaesthesia, on postoperative course.

Stimulus registration in anaesthetized patients has also been demonstrated with indirect or implicit memory tests. Patients who had been presented with verbal stimuli during surgery, showed a facilitation or change in performance on postoperative tasks that could only be attributed to intraoperative information-processing. Roorda-Hrdličková, Wolters, Bonke and Phaf [4] were among the first to demonstrate implicit memory for words presented during anaesthesia. Chapter 6 presents a replication study—with a different anaesthetic technique—initiated to validate their findings.

Brain-injured patients with severe amnesia show intact performance on free-association tasks which involve familiar linguistic idioms, but not on tasks based on recombinations of these idioms [5]. Kihlstrom and Schacter [1] have drawn an analogy between the implicit memory abilities of the patient with organic amnesia and those anaesthetized. They argued that cognitive processing under anaesthesia reflects automatic activation of old semantic knowledge, which makes pre-existing representations temporarily more accessible in postoperative memory. Virtually all studies of implicit memory in anaesthesia have used this activation paradigm. However, it is possible that new learning, i.e., the formation of new verbal associations in memory, also occurs in anaesthetized patients. Such learning has been found in both normal subjects and brain-injured patients with amnesia, using the mere exposure phenomenon [6] and the reading of degraded words [7]. Chapters 7 and 8 describe two experiments—each with a different anaesthetic technique—in which the possibility of new verbal learning under anaesthesia was examined.

References

1. Kihlstrom JF, Schacter DL. Anaesthesia, amnesia, and the cognitive unconscious. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 21-44.

2. Bonke B. Psychological consequences of so-called unconscious perception and awareness in anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990, 197-218.

3. Freud A. *Normality and Pathology in Childhood: Assessments of Development.* New York: International Universities Press, 1965.

4. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 150-155.

5. Schacter DL, Graf P. Preserved learning in amnesic patients: Perspectives from research on direct priming. *Journal of Clinical and Experimental Neuropsychology* 1986; *8:* 727-743.

6. Johnson MK, Kim JK, Risse G. Do alcoholic Korsakoff's syndrome patients acquire affective reactions? *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1985; *11:* 27-36.

7. Moscovitch M, Winocur G, McLachlan D. memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology* (General) 1986; *115:* 331-347.

Chapter 5

The effect of different types of intra-anaesthetic suggestions on post-operative course

M. Jelicic, B. Bonke and K. Millar

Abstract

A double-blind, randomized study was conducted to examine the effect of different types of therapeutic suggestions, administered during general anaesthesia, on postoperative course. 82 Patients undergoing cholecystectomy were intraoperatively exposed to (A) affirmative and nonaffirmative suggestions, (B) affirmative suggestions, (C) nonaffirmative suggestions or (D) an irrelevant story. Patients in condition (A) spent less time in hospital than patients in the other groups. No significant differences were demonstrated for subjective well-being measured on days 3 and 6 after surgery.

Introduction

There is evidence that sounds are registered in some areas of the cerebral cortex during general anaesthesia. Very few patients can consciously recall surgical events, but more sensitive assessments have demonstrated implicit memory for words presented during anaesthesia [1-3].

Anaesthetized patients may also respond to intraoperative therapeutic suggestions [4-6]. Patients who had been administered suggestions demonstrated a more favourable recovery and left the hospital sooner than those not exposed to therapeutic messages. However, there is a remarkable variety in the effect of suggestions administered during anaesthesia, on postoperative course. A number of studies reported a small or no effect of suggestions [4,7,8], whereas others yielded a large effect [5,6].

Possibly, some intraoperative suggestions have a larger impact on postoperative recovery than others. The essential ingredients of therapeutic suggestions are yet unknown. It is conceivable that affirmative positive suggestions (e.g., "You will feel relaxed and comfortable after surgery"), but not grammatical negatives (e.g., "You will *not* feel sick; you will *not* have any pain"), have a beneficial effect on postoperative well-being [9,10].

The present study was designed to investigate the essential ingredients of therapeutic messages presented during general anaesthesia on postoperative recovery. We expected that patients administered affirmative positive suggestions would show a more favourable course than those exposed to either a mixture of affirmative and nonaffirmative suggestions, nonaffirmative suggestions as such, or an irrelevant story.

Patients and methods

Eighty-two patients scheduled for elective cholecystectomy under general anaesthesia at a general hospital in Amsterdam, were studied after informed consent. They were 59 females and 23 males (mean age 55.2 yr; range 21-79). None had hearing problems, or a history of alcohol or psycho-active drug abuse. The patients were randomly, and double-blind, allocated to one of four groups (see below).

From time of skin incision, all patients were played an audiotape with seaside sounds, as a filler sound. Five minutes after first incision, the patients were presented with text fragments for 1 min, followed by 4 min of seaside sounds. This sequence was repeated continuously and was stopped at the time of wound closure. Seaside sounds were again administered from the closure of the peritoneum until the moment of extubation. In the first group (Mixed Suggestions [MS]), patients were exposed to affirmative suggestions, such as: "You are completely relaxed (. . .) After the operation you will feel comfortable, and you will heal quickly. . .," followed by therapeutic nonaffirmative suggestions: "You are *not* tense (. . .) After the operation you will *not* feel any nausea, and you will *not* feel bad. . ." In the second (Affirmative suggestions [AS]) and third (Nonaffirmative Suggestions [NS]) groups patients received affirmative suggestions and nonaffirmative suggestions, respectively. In the fourth group (Irrelevant Story [IS]), patients were presented with an irrelevant story, i.e., excerpts from a cookery book.

Anaesthesia was induced with thiopentone, droperidol, and sufentanil or fentanyl. Maintenance was with 66% nitrous oxide in oxygen. Atracurium or pancuronium were used for muscle relaxation. Additional sufentanil (or fentanyl) was given when there were signs of light anaesthesia. No volatile anesthetics were used.

On the 3rd day after surgery all patients were asked about any conscious recall of surgical events. The postoperative course was evaluated by means of the following variables: a global assessment of subjective well-being and duration of postoperative stay. On the 3rd and 6th days after the operation, three 5-point rating scales measuring different aspects of subjective well-being (i.e., general well-being, general health, stress) were administered, which were subsequently collapsed into one global score for each of the two time periods, i.e., "favourable," "intermediate," and "unfavourable" (adapted from [4,7]); duration of postoperative stay was registered after discharge from the hospital. Only three variables were selected as dependent variables to reduce the probability of type I error. We opted for subjective well-being and postoperative hospital stay as outcome variables because these indices were considered to provide overall assessments of postoperative recovery.

The Chi-square test for contingency tables and the Kruskal-Wallis non-parametric test were used to evaluate differences between groups. The Kruskal-Wallis test was used instead of ANOVA because our quantitative data were not normally distributed. Bonferroni's correction for Type I error was used and alpha was set at 0.0167 (i.e., 0.05 divided by 3).

Results

None of the patients reported any memories of intraoperative events. Table 1 summarizes potentially confounding variables: no significant differences between the four groups were found on the variables sex, age, ward, number of previous operations, level of experience of the surgeon, ASA grade, duration of operation, amount of blood loss, and preoperative anxiety (all p's > 0.15).

Table 2 shows the dependent variables for the four groups. No significant differences were found for well-being on the 3rd and 6th days. Patients in the mixed suggestion [MS] group spent significantly less time in hospital than patients in the other groups ($p = 0.0135$). The frequency distribution of postoperative stay for the four groups is presented in Figure 1.

Table 1. *Potentially confounding variables. n = Total number of patients in each group. Upper part of table: distribution of number of patients; test-statistic = Chi-square for contingency table. Lower part of table: median values of a variable; test-statistic = Chi-square based upon Kruskal-Wallis non-parametric test corrected for ties. MS = mixed suggestions; AS = affirmative suggestions; NS = nonaffirmative suggestions; IS = irrelevant story.*

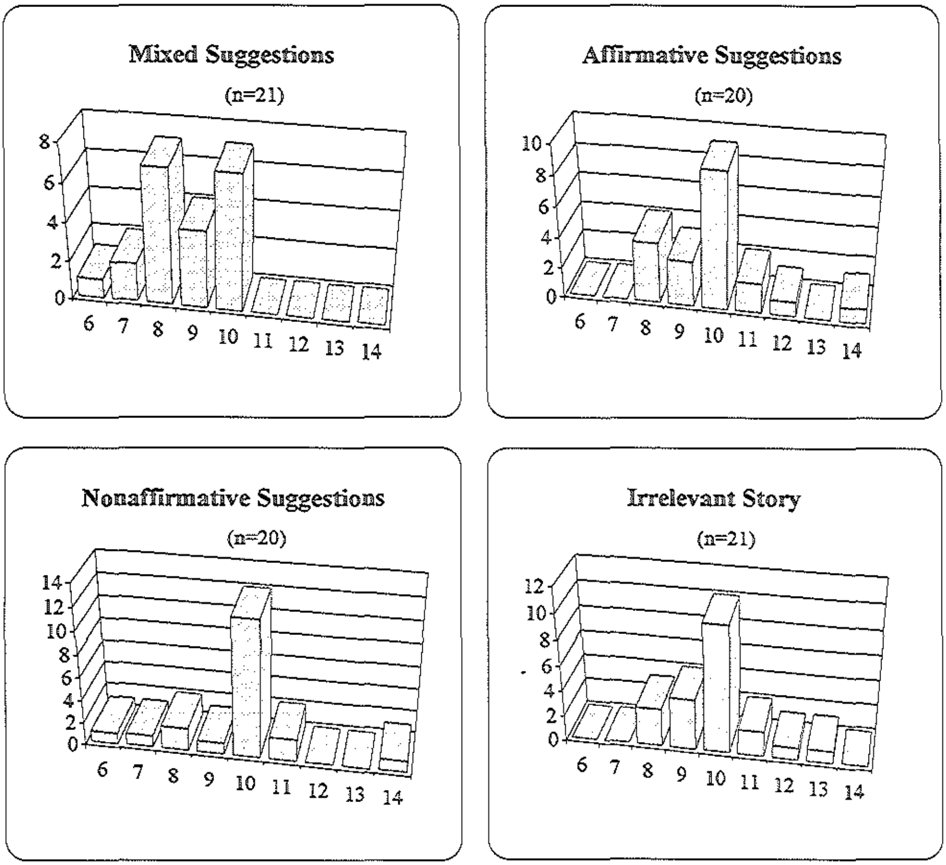
	MS (*n*=21)	AS (*n*=20)	NS (*n*=20)	IS (*n*=21)	χ^2	df	p
Sex							
M	6	7	7	3	2.93	3	0.40
F	15	13	13	18			
Ward							
I	11	6	8	7	3.40	6	0.76
II	7	9	8	11			
III	3	5	4	3			
Experience of surgeon							
High	13	10	12	11	0.83	3	0.83
Low	8	10	8	10			
ASA grade							
I	11	11	11	16	3.65	6	0.72
II	7	7	6	4			
III	3	2	3	1			
Age (yr)	57	60.5	58	58	1.70	3	0.64
Number of previous operations	1	1	1	1	2.08	3	0.56
Duration of operation (min)	57	62	60	57	0.40	3	0.93
Blood loss (ml)	150	250	250	200	5.06	3	0.17
Preoperative anxiety (STAI)	46	46	45	44	0.79	3	0.85

Table 2. *Dependent variables. n = Numbers of patients in each group. Upper part of table: distribution of numbers of patients on the variables Well-being 3rd day and 6th day; test statistic = Chi-square for contingency table. Lower part of table: median value of the variable Postoperative hospital stay; test statistic = Chi-square based upon Kruskal Wallis non-parametric test corrected for ties. MS = mixed suggestions; AS = affirmative suggestions; NS = nonaffirmative suggestions; IS = irrelevant story.*

	MS (*n*=21)	AS (*n*=20)	NS (*n*=20)	IS (*n*=21)	χ^2	df	P
Well-being 3rd day							
Favourable	9	9	6	5	4.05	6	0.67
Medium	6	7	6	7			
Unfavourable	6	4	8	9			
Well-being 6th day							
Favourable	9*	4	6*	11	6.09	6	0.41
Medium	6	11	8	7			
Unfavourable	5	5	5	3			
Postoperative hospital stay (days)	9	10	10	10	10.69	3	0.0135

*One patient omitted (already discharged)

Figure 1. *Frequency distribution of postoperative stay in hospital for the four groups. Note: one patient in the nonaffirmative suggestions group developed a serious postoperative complication and left the hospital after 22 days. For reasons of lay-out, we decided to display this patient as having left the hospital after 14 days.*



Discussion

Different types of therapeutic suggestions administered during general anaesthesia, have different effects on postoperative course. Patients who had been exposed to both affirmative and nonaffirmative suggestions spent less time in hospital (Mean [SEM] days in hospital 8.67 [0.26]) than those who had been presented with a) affirmative suggestions or b) nonaffirmative suggestions or c) an irrelevant story (Mean [SEM] days in hospital: 9.85 [0.33], 10.10 [0.69], and 9.86 [0.27] respectively). Contrary to our expectations, intraoperative suggestions seem to accelerate postoperative recovery only when they contain both affirmative and nonaffirmative statements.

It is worth noting, however, that the MS group differed slightly, though insignificantly, from the other groups in some of the potentially confounding variables. Patients in this group were a little younger, had had a somewhat shorter lasting operation and had lost a little less blood (Table 1). Theoretically, these lower values could have yielded an effect on postoperative hospital stay beyond the effect of the suggestions. Therefore, correlations were calculated between age, duration of operation and blood loss on the one hand, and hospital stay on the other. These were all low and not significant (0.23, 0.16 and 0.05, respectively), making it unlikely that the shorter hospital stay in the MS group was caused by initial differences between the groups. The reduced hospital stay in the MS group also cannot be explained by a greater exposure to stimuli during anaesthesia. All patients were intraoperatively presented with repeated sequences of one minute text followed by four minutes of seaside sounds.

Our study involved a number of surgeons, who all used their own implicit discharge criteria. One could therefore argue that differences in discharge criteria may have accounted for the shorter hospital stay in the MS group. However, this seems unlikely since the patients were randomly allocated to the four conditions. Moreover, we found no differences between the groups with regard to seniority of surgeons (see Table 1).

It remains to be explained why mixed suggestions produced the best result. Previous studies with positive effects [4-6] all used suggestions of the mixed type in comparison with sounds from the operating theatre, noise, nonsense suggestions, or a blank tape. This leaves us in doubt why, in the present study, parts of the suggestions (the "ingredients") seemed ineffective of themselves. There is a possibility that, although we applied the Bonferroni correction, the present outcome is due to chance. Further research into the effectiveness of different therapeutic suggestions seems necessary.

References

1. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory test: In: *Memory and Awareness in Anaesthesia.* Bonke B, Fitch W, Millar K, eds. Amsterdam: Swets & Zeitlinger, 1990: 150-155.

2. Kihlstrom JF, Schacter DL, Cork RC, Hurt CA, Behr SE. Implicit and explicit memory following surgical anesthesia. *Psychological Science* 1990; *1:* 303-306.

3. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Human learning during general anaesthesia and surgery. *British Journal of Anaesthesia* 1991; *66:* 170-178.

4. Bonke B, Schmitz PIM, Verhage F, Zwaveling A. Clinical study of so-called unconscious perception during general anaesthesia. *British Journal of Anaesthesia* 1986; *58:* 957-964.

5. Evans C, Richardson PH. Improved recovery and reduced postoperative stay after therapeutic suggestions during general anaesthesia. *Lancet* 1988; *ii:* 491-493.

6. McLintock TTC, Aitken H, Downie CFA, Kenny GNC. Postoperative analgesic requirements in patients exposed to positive intraoperative suggestions. *British Medical Journal* 1990; *301:* 788-790.

7. Boeke S, Bonke B, Bouwhuis-Hoogerwerf ML, Bovill JG, Zwaveling A. Effects of sounds presented during general anaesthesia on postoperative course. *British Journal of Anaesthesia* 1988; *60:* 697-702.

8. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Efficacy of therapeutic suggestions for improved postoperative recovery presented during general anesthesia. *Anesthesiology* 1991; *75:* 746-755.

9. Bonke B. Psychological consequences of so-called unconscious perception and awareness in anaesthesia. *Memory and Awareness in Anaesthesia.* Bonke B, Fitch W, Millar K, eds. Amsterdam: Swets & Zeitlinger, 1990: 197-218.

10. Bennett HL. Influencing the brain with information during general anaesthesia: A theory of "unconscious hearing." *Memory and Awareness in Anaesthesia.* Bonke B, Fitch W, Millar K, eds. Amsterdam: Swets & Zeitlinger, 1990: 50-56.

Chapter 6

Implicit memory for words presented during anaesthesia

M. Jelicic, G. Wolters, R.H. Phaf and B. Bonke.

Abstract

Tests for implicit memory seem to be rather insensitive to the amount of attention given to stimuli during study. In the experiment reported here, the effect of a complete absence of attention during presentation of stimulus material on implicit memory performance was studied. Surgical patients were auditorily presented with exemplars of word categories during general anaesthesia. At the earliest convenient time after surgery they were requested to generate category exemplars. Although none of the patients expressed any conscious recollection of events during the surgical episode, experimental patients generated significantly more critical exemplars than a control group. Apparently, information presented during anaesthesia can influence postoperative performance in an implicit memory task. Repetition priming seems possible even in the absence of attentional processing at the time of encoding. It is argued that the nature of the unattended encoding process can best be described as the automatic activation and strengthening of pre-existing memory representations.

Introduction

Repeated presentation of stimuli facilitates performance in tasks such as word completion and perceptual identification. This effect is found even after long intervals and in the absence of any conscious recollection of the prior presentation. Tests measuring such repetition priming effects have been labeled implicit memory tests [1]. In contrast, standard tests of memory, like recall and recognition, always require an explicit reference to and recollection of a prior learning episode. Therefore, they are referred to as explicit memory tests.

The distinction between explicit and implicit memory tests is important, because a large number of experimental manipulations and conditions seem to affect performance in both types of test differently (see [2,3] for reviews). For example, manipulations of "level of processing," study time, retention interval, interference conditions, alcoholic intoxication, and posthypnotic suggestions, as well as increasing age of subjects, have large effects on explicit memory performance, but hardly any effect on implicit memory tests. In contrast, implicit memory performance seems to be highly sensitive to physical dissimilarities in the presentation of stimuli at study and test, whereas explicit memory tests are rather robust with regard to such variations. Other manipulations even show cross-over dissociation effects. Generation of target items by the subject, for example, leads to better performance in explicit tests than simply reading these target items, but the reverse result has been observed in implicit tests. Also, high frequency words—as opposed to low frequency words—are better recalled, but less often completed in a word-completion test. Theoretically, these dissociation effects are of great interest because they may provide new insights into the functional and structural characteristics of memory.

This study addresses still another, probably important, potential dissociation factor, namely degree of attention during study. It is generally assumed that attentional processing is a prerequisite for, and critically determines, explicit memory performance [4,5]. In contrast, repetition priming seems to be independent of the level of attention during processing, and seems to occur even in the absence of any attentional encoding. These are two different questions. The first is whether implicit memory is insensitive to a manipulation of level of attention to which an explicit memory test is sensitive. This can be studied by varying the amount of attention during study [6]. The second question is whether implicit memory effects are found even when subjects do not attend to stimuli at all, i.e., when processing is completely automatic. This latter question is put to test here.

Several studies have shown that if the level of attention during encoding is suppressed to a degree where explicit memory performance is reduced to chance level, implicit memory is still present. For example, Eich [7] had subjects shadow a passage of text presented to one ear, whereas word pairs were simultaneously presented to the other unattended ear. The word pairs consisted of a homophone and a word that biased its less common interpretation. The homophones could not be recognized. Yet implicit memory performance, measured by determining the likelihood of producing the biased interpretation of the homophones in a later spelling test, was clearly present. Similar results were obtained in tests measuring affective preference [8].

Although these results are suggestive, they do not allow the conclusion that attentional processing is not necessary for the establishment of implicit memory, since Holender [9] has argued that instructional or procedural manipulations may be insufficient to exert complete control over the level of attention. One situation, however, that makes it almost certain that subjects are unable to attend to information presented to them, is when they are subjected to general surgical anaesthesia. Roorda-Hrdličková, Wolters, Bonke and Phaf [10] studied implicit memory in such a situation. Eighty-one patients scheduled for surgery under general anaesthesia were randomly assigned to an experimental and a control condition. While anaesthetized, tape recordings were played to all subjects over headphones starting 15 min after the first incision. The tape for the experimental group contained repeated recordings of two words from each of two semantic categories. Patients in the control group were played a tape containing only neutral sounds. After recovery, none of the patients could remember having heard either words or sounds. When asked to name the first exemplars of the experimental categories that came to mind, however, the patients in the experimental group generated almost three times as many "target" exemplars than the patients in the control group. It was concluded that these results indicated the existence of an automatic activation process that does not require attention. This process presumably strengthens existing memory representations which facilitates later access.

Since then, Ghoneim, Block, Sum-Ping, Ali and Hoffman [11], and Kihlstrom, Schacter, Cork, Hurt and Behr [12] have published results also showing implicit memory for auditory stimuli presented during anaesthesia. They found, however, only small effects. These differences in effect may be explained by the less than optimal conditions in the latter two studies. Kihlstrom etal. [12], for example, stated that their implicit memory effect was reduced when explicit tests (free and cued recall) preceded the implicit test. Since this was the case in half of their subjects, the overall implicit memory effect was consequently reduced. Moreover, their stimuli consisted of 15 words (later used as cues) and their most frequent associates (target words). Therefore, there was only limited room for improvement in the free association test used for measuring implicit memory. Ghoneim et al. [11] combined auditory presentation with a "visual" word-completion test. There is ample evidence that implicit memory performance is highly sensitive to physical dissimilarities between presentation and test conditions [3,13]. The modality shift in their study may have reduced the experimental effect.

One study [14], failed to show evidence for implicit retention of material presented during anaesthesia. The methodology of this study, however, was less than optimal. First, a relatively large amount of auditory information was presented only once, and just for a short time period. Probably, stimuli have to be presented at least a number of times before an effect can be found. Second, patients were not prevented from picking up other possibly interfering words or phrases before and after stimulus presentation. Third, postoperative testing did not take place before the fourth or fifth day after the operation. Such a long retention interval may have led to the disappearance of any effect, not only due to the elapsed time, but also to interfering conversation. It may be noted, though, that an absence of susceptibility to interference, and a relative insensitivity to the length of the retention interval in implicit memory tests, have been suggested as other instances of a dissociation with explicit memory tests. Many studies, however, do show a decline in implicit memory effects over time. Moreover, this decline seems to be steeper for verbal material [15,16], where relatively much interference can be expected from everyday verbal activity, than for other types of material such as pictures or reading inverted text where interfering activities are less obvious [17,18]. This is in accordance with observations by Graf, Squire and Mandler [19] and McClelland and Rumelhart [20] that word frequency and number of response alternatives may adversely affect the duration of a repetition priming effect.

Given the nature and the magnitude of the effect reported by Roorda-Hrdličková et al. [10], a replication study to validate their results seemed to be in order. The same experimental paradigm was used, but the study was carried out by a different experimenter, in a different hospital, and with a different anaesthetic technique. The latter change is relevant since auditory information processing may be differentially affected by different anaesthetic agents [21].

Method

Subjects

Fifty surgical patients, scheduled for elective procedures under general anaesthesia, participated in the experiment after informed consent. They were 41 females and 9 males, mean age 37.9 yr (range 19-71 yr). None of the patients had hearing difficulties, or a history of alcohol- or psychoactive drug abuse. The patients were randomly, and evenly, allocated to the experimental or control condition in a double-blind fashion.

Material

The words presented during anaesthesia were familiar exemplars of the categories "fruit" (pear and banana) and "colours" (yellow and green). Roorda-Hrdličková et al. [10] had selected these target words on the basis of a preliminary study in which spontaneous generation frequencies of exemplars from several categories had been determined. The selected exemplars were familiar, but not the most frequently generated, exemplars of the two categories. During postoperative testing, a third category "vegetables" was used as a control category.

Procedure

In the afternoon before surgery each patient completed the state version of the State-Trait Anxiety Inventory [22] to assess preoperative anxiety. From the time of skin incision, all patients were played an audiotape via headphones, using a Uher-CR210 tape recorder. The headphones made sounds from the operating theatre inaudible to the patient and prevented the content of the tape being overheard by the experimenter or others. For the control group the tape contained 20 min of seaside sounds. For the experimental group it comprised 5 min of seaside sounds followed by 30 presentations of the four target words spoken by a male voice, for 15 min. The target words (yellow, banana, green and pear) had been tape-recorded, in this order, at a speed of one word every 1.5 s, preceded by a warning phrase: "Please, listen carefully . . .," and copied on tape 30 times with an interval between series of about 20 s. The words were presented 30 times to strengthen the experimental effect. After 20 min, a different tape with seaside sounds was played to all patients for the remainder of the operation. The actual tapes for both groups were visually identical and had been coded A and B by someone not involved in the experiment. Only after all data had been collected were the codes broken.

Anaesthesia was induced with thiopentone (250-500 mg) and droperidol (3-5 mg). Atracurium or pancuronium was used for muscle relaxation. Maintenance took place with 66% nitrous oxide in oxygen, supplemented with either sufentanil or fentanyl as required. No volatile anaesthetics were used.

Each patient was interviewed at the earliest convenient time after surgery, i.e., when they had fully regained consciousness and were able to communicate (the mean interval between start of 2nd tape and postoperative testing was 80.6 min, with a range of 30-179 min). Patients were first asked about any recall of intraoperative events. They were then invited to name the first three exemplars of the categories "vegetables" (as a control), "fruit" and "colours" that came to mind. Generated exemplars corresponding with one of the target words were scored as "hits." A maximum of four hits (all target words) could thus be obtained.

A one-tailed Student's t-test was carried out to determine whether the two groups differed in the number of generated hits.

Results

The experimental and control groups were comparable with respect to age, duration of surgery, preoperative anxiety and number of previous operations under general anaesthesia (two-tailed Student's t-tests; all p-values > 0.20). None of the patients reported any recall of intraoperative events. The mean numbers of hits (standard error in parentheses) were 2.40 (0.18) for the experimental condition and 1.84 (0.20) for the control condition ($t = 2.8$; $df = 48$; $p < 0.025$, one-tailed). For the category "fruit" the number of hits were 1.20 (0.12) and 1.00 (0.14), and for "colours" 1.20 (0.10) and 0.84 (0.13) respectively. There was no significant difference between groups with respect to exemplars generated for the non-experimental category "vegetables" (two-tailed Student's t-test for the frequencies of the five most often mentioned exemplars; $t = 0.95$; $df = 48$; $p < 0.35$). Post-hoc analyses showed nonsignificant, low correlations between the number of hits in the experimental group on the one hand, and age, interval between presentation and testing, preoperative anxiety and number of previous operations under general anaesthesia on the other (correlations varying from -0.25 to 0.11, none of these being statistically significant).

Discussion

The results of this study are in accordance with those of Roorda-Hrdličková et al. [10], Ghoneim et al. [11], and Kihlstrom et al. [12], who all used different anaesthetic procedures. It is, therefore, unlikely that information processing and memory storage under general anaesthesia are restricted to particular anaesthetic cocktails.

Although we used the same experimental procedures as before, the difference in performance between experimental and control groups in the Roorda-Hrdličková et al. [10] study was considerably larger than in the study reported here. Both studies are comparable with respect to the mean number of generated hits in the experimental condition (2.35 vs. 2.40). The control patients in the earlier study, however, produced remarkably fewer hits than in ours (means:

0.79 vs. 1.84, respectively). This difference can, of course, be a consequence of sampling error. Another possible explanation is based on the finding that the majority of patients in the study by Roorda-Hrdličková et al. [10] had intermediate or major surgery, whereas the best part of our patients underwent minor surgical procedures. Since major surgery normally requires long periods of anaesthesia, residual anaesthetic agents may have been present in these patients at the time of testing. This may have produced more stereotyped responses, especially in the control group. There was, in fact, a tendency in their control group to generate the most frequent exemplars more often than was the case in the preliminary normative study. This, of course, reduces the probability of naming "target" exemplars. We did not find this tendency in our study (the number of patients with major surgery was too small to allow statistical analysis).

The present study and the studies discussed in the introduction, provide convincing evidence for implicit memory during anaesthesia. Apparently, information can be encoded and stored automatically, i.e., without controlled attention being paid to the information. The results of these anaesthesia studies show a clear dissociation effect: processing auditory information during anaesthesia is not sufficient for explicit retention, but it does allow implicit memory performance. Although different explanations of dissociation effects between explicit and implicit memory performance have been suggested (multiple memory systems [23,24], or study-test compatibility [13]), the dissociation as shown in this study seems to be most compatible with an explanation suggested by Graf and Mandler [25]. They distinguished between two learning mechanisms: elaboration and activation learning. Elaboration learning presumably results in the formation of new associations between stimuli and their context which is a prerequisite for explicit memory performance. This type of learning requires active attentional processing. In contrast, activation learning does not require attention and consists of the automatic activation and strengthening of old, pre-existing representations. This strengthening subsequently allows faster access to these representations which enhances performance in implicit memory tests. We suggest that the nature of the unattended encoding process taking place during anaesthesia can be described most parsimoniously by such an activation learning mechanism. This does not imply, however, that the distinction between activation and elaboration learning can explain all dissociation effects. There is clear evidence, for example, that study-test compatibility factors also have to be taken into account. Moreover, it should be noted that even when attention during processing is involved in dissociation effects, there is not a simple and direct relationship between elaboration and activation learning, and explicit and implicit memory performance, respectively. Attentive processing during elaboration learning not only creates new associations, but also activates and strengthens pre-existing representations. Both these newly formed representations, and the pre-existing ones that were strengthened may facilitate performance in compatible implicit memory tests [26]. Therefore, both activation and elaboration learning may affect implicit memory performance, but only the latter affects explicit memory performance [27].

The finding that unattended processing affects performance in a category-exemplar-generation task, shows that activation learning during anaesthesia is not restricted to low level "perceptual" representations, but also affects high level "conceptual" representations. These representational levels probably should be regarded as a hierarchy constituting a single stimulus representation complex. The activation learning process as described here raises the suggestion that it seems to be independent of attention. There is some supporting evidence for independence in studies where divided attention impaired recall but did not affect implicit memory [6,28]. Moreover, research on drug induced amnesia showed that attention/arousal-affecting drugs, such as diazepam and scopolamine, reduced performance in recall and recognition but had little or no effect on repetition priming [29,30]. Other studies, however, showed at least a weak relationship between attention and implicit memory performance [31-33]. It is therefore too early to draw definite conclusions on the relationship of activation learning and attention. The anaesthesia studies clearly show that implicit memory effects occur in the absence of attention. Future research in this area may focus on the effects of specific manipulations, like number of presentations, delay between presentation and test, and stimulus familiarity, on the size of the repetition priming effect.

References

1. Graf P, Schacter DL. Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1985; *11:* 501-518.

2. Schacter DL. Implicit memory: History and current status. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1987; *13:* 501-518.

3. Richardson-Klavehn A, Bjork RA. Measures of memory. *Annual Review of Psychology* 1988; *39:* 475-543.

4. Shiffrin RM, Schneider W. Controlled and automatic human information processing: II Perceptual learning, automatic attending, and a general theory. *Psychological Review* 1977; *84:* 127-190.

5. Hasher L, Zacks RT. Automatic and effortful processes in memory. *Journal of Experimental Psychology* (General) 1979; *108:* 356-388.

6. Parkin AJ, Russo R. Implicit and explicit memory and the automatic/effortful distinction. *European Journal of Cognitive Psychology* 1990; *2:* 71-80.

7. Eich E. Memory for unattended events: Remembering with and without awareness. *Memory & Cognition* 1984; *12:* 105-111.

8. Kunst-Wilson WR, Zajonc RB. Affective discrimination of stimuli that are not recognized. *Science* 1980; *207:* 557-558.

9. Holender D. Semantic activation without conscious identification in dichotic listening, parafoveal vision, and visual masking: A survey and appraisal. *The Behavioral and Brain Sciences* 1986; *9:* 1-66.

10. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 151-155.

11. Ghoneim MM, Block RI, Sum-Ping ST, Ali MA, Hoffman JG. Learning without recall during general anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 161-169.

12. Kihlstrom JF, Schacter DL, Cork RC, Hurt CA, Behr SE. Implicit and explicit memory following surgical anaesthesia. *Psychological Science* 1990; *1:* 303-306.

13. Roediger HL, Blaxton TA. Effects of varying modality, surface features, and retention interval on word fragment completion. *Memory & Cognition* 1987; 15: 379-388.

14. Eich E, Reeves JL, Katz RL. Anaesthesia, amnesia, and the memory/awareness distinction. *Anesthesia and Analgesia* 1985; *64:* 1143-1148.

15. Jacoby LL. Perceptual enhancement: Persistent effects of an experience. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1983; *9:* 21-38.

16. Salasoo A, Shiffrin RM, Feustel TC. Building permanent memory codes: Codification and repetition effects in word identification. *Journal of Experimental Psychology* (General) 1985; *114:* 50-77.

17. Kolers PA. Reading a year later. *Journal of Experimental Psychology* (Human Learning and Memory) 1976; *2:* 554-565.

18. Moscovitch M, Winocur G, McLachlan D. Memory as assessed by recognition and reading time in normal and memory impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology* (General) 1986; *115:* 331-347.

19. Graf P, Squire LR, Mandler G. The information that amnesic patients do not forget. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1984; *10:* 164-178.

20. McClelland JL, Rumelhart DE. A distributed model of human learning and memory. In: McClelland JL, Rumelhart DE, and the PDP Research Group, eds. *Parallel Distributed Processing: Explorations in the Microstructure of Cognition.* Vol.2, Psychological and Biological Models. Cambridge, MA: MIT Press, 1986: 170-215.

21. Jones JG, Konieczko K. Hearing and memory in anaesthetised patients. *British Medical Journal* 1986; *292:* 1291-1293.

22. Spielberger CS, Gorsuch RC, Lushene RE. *Manual for the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press, 1970.

23. Tulving E. *Elements of Episodic Memory.* Oxford: Oxford University Press, 1983.

24. Squire LR, Cohen NJ. Human memory and amnesia. In: McGaugh J, Lynch G, Weinberger N, eds. *Proceedings of the Conference on the Neurobiology of Learning and Memory.* New York: Guilford Press, 1984: 3-64.

25. Graf P, Mandler G. Activation makes words more accessible, but not necessarily more retrievable. *Journal of Verbal Learning and Verbal Behavior* 1984; *23:* 553-568.

26. Schacter DL, McGlynn SM. Implicit memory: Effects of elaboration depend on unitization. *American Journal of Psychology* 1989; *102:* 151-181.

27. Wolters G, Phaf RH. Explicit and implicit measures of memory: Evidence for two learning mechanisms. In: B. Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 57-63.

28. Smith ME, Oscar-Berman M. Repetition priming of words and pseudowords in divided attention and in amnesia. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1990; *16:* 1033-1042.

29. Fang JC, Hinrichs JV, Ghoneim MM. Diazepam and memory: Evidence for spared memory function. *Pharmacology Biochemistry and Behavior* 1987; *28:* 347-352.

30. Nissen MJ, Knopman DS, Schacter DL. Neurochemical dissociation of memory systems. *Neurology* 1987; *37:* 789-794.

31. Oliphant GW. Repetition and recency effects in word recognition. *Australian Journal of Psychology* 1983; *35:* 393-403.

32. Anooshian LJ. Effects of attentive encoding on analytic and nonanalytic processing in implicit and explicit retrieval tasks. *Bulletin of the Psychonomic Society* 1989; *27:* 5-8.

33. Neill WT, Beck JL, Bottalico KS, Molloy RD. Effects of intentional versus incidental learning on explicit and implicit tests of memory. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1990; *16:* 457-463.

Chapter 7

Unconscious learning during anaesthesia

M. Jelicic, A. de Roode, J.G. Bovill and B. Bonke

Abstract

Forty-three surgical patients were, during general anaesthesia, presented (via headphones) with either statements about common facts of some years ago (group A), or new verbal associations, i.e., the names of fictitious, nonfamous people (group B). None had any recall of intraoperative events. In a postoperative test of indirect memory, patients in group A answered more questions about the "common facts" correctly than those in group B ($p < 0.005$), which reflects the activation of pre-existing knowledge. Furthermore, patients in group B designated more "nonfamous names" as famous (thus falsely attributing fame) than patients in group A ($p < 0.001$), which demonstrates that information-processing during anaesthesia can also take place as unconscious learning.

Introduction

There is reason to believe that some form of information-processing occurs during the state of unconsciousness induced by general anaesthesia. Studies which used indirect, or implicit, memory tests have demonstrated stimulus registration without conscious awareness during anaesthesia [1-3], though not under all circumstances [4,5]. In contrast with traditional, direct tests such as recall and recognition, tests of indirect memory do not refer to conscious recollection of a previous learning episode but bring about a change in task performance attributable to a learning period [6]. Roorda-Hrdličková and colleagues [1] were among the first to demonstrate indirect memory for neutral words presented during anaesthesia. Their findings were recently replicated and expanded [2,3].

It has been suggested that intraoperative stimulus registration reflects automatic activation of old semantic knowledge, which makes pre-existing representations temporarily more accessible in postoperative memory [7]. Practically all studies of cognition and anaesthesia employing indirect memory paradigms have involved the activation of pre-existing representations in memory. However, it cannot be excluded that unconscious learning, i.e., the formation of new verbal associations in memory, also occurs in anaesthetized patients. Such indirect learning has been demonstrated—with indirect memory tests—in both normal subjects and patients with organic amnesias [8,9]. The present study was designed to investigate whether or not anaesthetized patients are capable of learning new verbal associations. The design of the study also permitted a replication of the activation paradigm.

Patients and Methods

Patients

During a five months period, adult patients (18-50 yr, ASA I-II) scheduled for strabismus surgery under standardized general anaesthesia, were studied after informed consent. The study was approved by the local medical ethics committee. Patients with hearing difficulties or a history of alcohol abuse, and those who used psychoactive drugs were excluded from the study.

Procedure

The patients were randomly allocated to two groups, and the study was performed in a double-blind fashion. Preoperative anxiety was assessed on the afternoon before surgery using the state version of the State-Trait Anxiety Inventory [10]. Immediately after induction of anaesthesia, all patients were played an audio tape with natural seaside sounds (waves, gulls), via headphones, using a Uher CR 210 tape recorder. The headphones prevented both patients hearing sounds from the operating room and the experimenters hearing the contents of the tape. Five min after first surgical incision, the seaside tape was replaced with one containing 10 repeated recordings, over 15 min. For group A the recording comprised 10 statements about common facts of some years previously (e.g., "Queen Beatrix came to the throne in 1980"). A pilot study ($n = 53$) in out-patients had shown that details of these selected common facts had largely been forgotten. For group B the recording contained the names of ten fictitious non-famous people (e.g., "Martin Petersen"). One series of the common facts on the tape for group A lasted approximately 90 sec; average duration of each statement was 6 sec; interval between statements was 3 sec. For group B: one series of names lasted approximately 90 sec; average duration of each name was 1.5 sec; interval between names was 7.5 sec. After the administration of experimental stimuli, the seaside tape was again played to the patients for the remainder of the operation.

Anaesthesia

For all patients the anaesthetic procedure used in this study was that which is common for day-case surgery. All anaesthetics were given by one of the authors (ADR). No sedative drugs were given preoperatively. During anaesthesia the E.C.G. was continuously registered and the arterial blood pressure (non-invasively), ventilation parameters, end-tidal carbon dioxide tension and oxygen saturation were monitored. Atropine 0.5 mg was given before induction. After three minutes preoxygenation anaesthesia was induced with alfentanil 20 $\mu g\ kg^{-1}$ and thiopental 4-5 $mg\ kg^{-1}$. When consciousness was lost, succinylcholine 1 $mg\ kg^{-1}$ was given and the trachea was intubated. Anaesthesia was maintained with 35% oxygen and 65% nitrous oxide. Additional boluses of alfentanil, 0.5-1 mg, were given when heart rate or arterial blood pressure increased by more than 10% of the preoperative value. Vecuronium 4-6 mg was given for muscle relaxation, with incremental doses of 1 mg every 20 min. Ventilation was adjusted to maintain an end-tidal carbon dioxide tension between 3.5-4.0 vol %. At the end of surgery atropine 0.5 mg and neostigmine 1 mg were given to reverse residual muscular blockade, and the nitrous oxide administration was discontinued. The trachea was extubated when patients were awake with satisfactory spontaneous ventilation. Median interval between the end of the experimental tape (common facts for Group A, fictitious names for Group B) and discontinuation of the nitrous oxide administration was 36 min (range: 0-85 min). The minimum duration of anaesthesia was 20 min, hence some patients did not hear the seaside tape again after the experimental tape. None of the experimental stimuli were administered after the administration of nitrous oxide had been stopped.

Interview and tests

All patients were interviewed—at the ward—as soon as possible after surgery (median interval between end of presentation of the experimental tape and postoperative testing: 176 min, range 104-291). They were first asked about any recall of intraoperative events: –"What is the last thing you remember from the period before the operation?" –"What is the first thing you remember from the period after the operation?" –"Is there anything you remember from the period in between?"

Next, patients were given 15 questions about past events. Ten of these questions related to the statements presented intraoperatively to group A (e.g., "When did Queen Beatrix come to the throne?"), and formed the indirect memory test for activation of pre-existing memory representations. Finally, the patients were asked to state whether each of 20 combinations of first names and surnames belonged to a famous person or not. Ten of these, making up the indirect test for the learning of new associations, were the nonfamous names presented to group B during surgery (e.g., "Martin Petersen"). The other ten were fillers, containing five new nonfamous names, and five new names of moderately famous people. Postoperative indirect memory for pre-existing memory representations (activation) would show up if patients from group A answered more questions about the common facts correctly than patients in group B. Indirect memory for new associations (learning) would be expressed if patients in group B designated more nonfamous names as famous than those in group A. In this case, nonfamous names—i.e., the unique combinations of first names and surnames—which lack any pre-existing memory representation, would have gained in familiarity as a result of a new memory trace (see [11,12] for more details about this test). Data were analysed with Student's t-tests for differences between groups.

Results

Twenty-five female and 18 male patients (mean age 32 yr, range 18-49) were enrolled in the study. Group A consisted of 21 patients, group B of 22 patients. There were no significant differences between the groups with respect to age, gender, number of previous operations, preoperative anxiety, duration of surgery, and interval between presentation of stimuli and testing. None of the patients had recall of any intraoperative events. Both indirect memory tests revealed evidence of information-processing during anaesthesia. Mean (SEM) number of correct answers on the common facts test was 5.2 (0.46) for group A, and 3.0 (0.57) for group B ($t = 3.03$, $df = 41$, $p < 0.005$; 95% CI for true difference: 0.74-3.72). Mean (SEM) number of the 10 nonfamous names that were designated as famous on the learning test was 1.6 (0.30) for group B, and 0.3 (0.10) for group A ($t = 4.06$, $df = 41$, $p < 0.001$; 95% CI for true difference: 0.65-1.95). (As a check on possible violations regarding the use of t-tests, the data were also analysed nonparametrically by Mann-Whitney's U-test corrected for ties, with similar results [$Z_U = -2.87$, $p < 0.005$ and $Z_U = -3.65$, $p < 0.0005$, for the common facts test and the famous names test, respectively]. We decided to present means and t-values here for reasons of clarity.) Neither for the five filler questions, nor for the filler names, was there a difference between groups that approached significance (t-tests: all p-values > 0.50). Proportions correct (for the common facts test) and proportions attributed fame (for the famous names test) for both experimental and filler items are presented in Table 1.

Discussion

Our results have both theoretical and practical significance. Kihlstrom and Schacter [7] hypothesized that anaesthetized patients are able to execute some highly automated information-processing functions, but probably not the higher cognitive processing required to encode an

Table 1. *Proportions correct (for the "common facts" test) and proportions attributed fame (for the "famous names" test) for the two groups, for experimental and filler items*[1].

	Group A (*n*=21)	Group B (*n*=22)	p(diff)
Common facts			
Experimental	0.52	0.30	<.005
Fillers[2]	0.68	0.72	.590
Names			
Experimental (nonfamous)	0.03	0.16	<.001
Fillers			
Famous	0.90	0.88	0.740
Nonfamous	0.02	0.04	0.740

[1]Group A had been administered a tape with the 10 experimental common facts, group B had heard the 10 experimental nonfamous names; p(diff) refers to p-values (t-tests for differences between means). Proportions are shown, instead of means, because the number of tested items differs between the various categories. [2]In order not to discourage patients, we selected as the five filler questions items which concerned facts that were easier to remember than the experimental ones. Thus, each patient was able to answer at least some questions correctly, hence the relatively large proportions for the fillers as compared with the proportions for the experimental facts.

entirely new memory trace. For this reason, indirect memory under anaesthesia was assumed to be limited to the activation of pre-existing representations in memory (see Jelicic et al. [13] for an extended discussion of this issue). Our results indicate that new associations may be formed in memory during anaesthesia. This suggests that some of the brain functions associated with verbal learning remain active during this state of unconsciousness, i.e., with a minimum amount of attention paid to the stimuli. Our patients did not receive any sedative drugs preoperatively, nor were any volatile anaesthetics used in the study. This may have contributed to our findings because anaesthesias with nitrous oxide, oxygen, and opiates are known to result in a relatively high incidence of conscious awareness. This incidence diminishes with the use of volatile anaesthetics or benzodiazepines [14]. Therefore, the possibility that auditory information is transmitted to the cerebral cortex may increase when N_2O/O_2 and alfentanil are used. Furthermore, benzodiazepines—frequently used as premedicant drugs—affect performance on direct, and to a lesser amount, indirect memory tasks [15]. Therefore, further studies are indicated to assess the effect of other anaesthetic techniques, including premedicant drugs and/or volatile anaesthetics. With a similar design as that used in the present study, groups of surgical patients can be tested with different anaesthesias, to be compared both among themselves, and with our results. Moreover, the demonstration that learning can take place during general anaesthesia raises the question as to what the level is up to which such learning can indeed be found.

Information-processing and memory storage under anaesthesia have important implications. Inappropriate or ambiguous remarks made during surgery may lead to adverse postoperative effects. Howard [16] described two patients who had developed a post-traumatic anxiety disorder as a result of unconscious perception of negative remarks made while under anaesthesia. The notion that a quite sophisticated form of memory storage (learning) may take place without any attention or consciousness makes clear why this can sometimes be the case.

References

1. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 150-155.

2. Jelicic M, Bonke B, Appelboom DK. Indirect memory for words presented during anaesthesia. *Lancet* 1990; *ii:* 249.

3. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Human learning during general anaesthesia and surgery. *British Journal of Anaesthesia* 1991; *66:* 170-178.

4. Bonke B, Van Dam ME, Van Kleef JW, Slijper FME. Implicit memory tested in children with inhalation anaesthesia. *Anaesthesia* (in press).

5. Winograd E, Sebel PS, Goldman WP, Clifton C, Lowdon JD. Indirect assessment of memory for music during anesthesia. *Journal of Clinical Anesthesiology* 1991; *3:* 276-279.

6. Richardson-Klavehn A, Bjork RA. Measures of memory. *Annual Review of Psychology* 1988; *39:* 475-543.

7. Kihlstrom JF, Schacter DL. Anaesthesia, amnesia, and the cognitive unconscious. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 21-44.

8. Moscovitch M, Winocur G, McLachlan D. Memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology* (General) 1986; *115:* 331-347.

9. Gordon B. Preserved learning of novel information in amnesia: Evidence for multiple memory systems. *Brain and Cognition* 1988; *7:* 257-282.

10. Spielberger CD, Gorsuch RL, Lushene RE. *Manual of the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press, 1970.

11. Jacoby LL, Kelley CM. Unconscious influences of memory for a prior event. *Personality and Social Psychology Bulletin* 1987; *13:* 314-336.

12. Jacoby LL, Woloshyn V, Kelley C. Becoming famous without being recognized: unconscious influences of memory produced by dividing attention. *Journal of Experimental Psychology* (General) 1989; *118:* 115-125.

13. Jelicic M, Wolters G, Phaf RH, Bonke B. Implicit memory for words presented during anaesthesia. *European Journal of Cognitive Psychology* 1992; *4:* 71-80.

14. Utting JE. Clinical aspects of awareness during anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 259-271.

15. Ghoneim MM, Mewaldt SP. Benzodiazepines and human memory: A review. *Anesthesiology* 1990; *72:* 926-938.

16. Howard JF. Incidents of auditory perception during anaesthesia with traumatic sequelae. *Medical Journal of Australia* 1987; *146:* 44-46.

Chapter 8

Implicit learning during enflurane anaesthesia in spontaneously breathing patients?

M. Jelicic, A.J. Asbury, K. Millar and B. Bonke

Abstract

Forty-one spontaneously breathing patients were, during enflurane anaesthesia, presented (via headphones) either with statements about common facts of some years ago, or new verbal associations, i.e., names of fictitious people. Postoperatively, there were no differences between the two groups with regard to questions about the common facts or attribution of fame to the fictitious people. This finding suggests that unconscious learning and activation are largely reduced during enflurane anaesthesia without neuromuscular blockade.

Introduction

Evidence suggests that some amount of auditory information-processing occurs under general anaesthesia. Experiments which used sensitive implicit memory tests have shown intraoperative registration of verbal stimuli without subsequent conscious recall [1-3]. Recall is an explicit test of memory and requires conscious remembering of a learning episode. Implicit memory tests, in contrast, do not refer to such conscious recollection but bring about a change in memory task performance which can be attributed to a previous learning period [4]. Some authors have drawn an analogy between patients who suffer from organic amnesias and anaesthetized patients [5,6]. Both have severely impaired explicit memory functions but relatively preserved implicit memory capabilities.

Most studies of cognition and anaesthesia employing implicit memory paradigms have involved the activation of old knowledge, which makes pre-existing representations temporarily more accessible in postoperative memory [6]. Very recently however, Jelicic, De Roode, Bovill and Bonke [7] reported evidence for true learning, i.e., the formation of new verbal associations in memory, during day-case anaesthesia with nitrous oxide/oxygen and alfentanil. However, since no volatile anaesthetic agents were used in their study, it remains uncertain whether or not learning of new information can take place under inhalation anaesthesia. Anaesthesia with nitrous oxide/oxygen and opioids is associated with a relatively high incidence of conscious awareness [8]. This incidence is much lower with inhalation anaesthesia, suggesting that the amount of information-processing in the cerebral cortex is reduced when volatile agents are used as adjuvants to nitrous oxide. Although two studies have demonstrated activation of pre-existing knowledge during anaesthesia with isoflurane [1,3], volatile anaesthetics might prevent the formation of new verbal associations in memory—a more sophisticated form of cognitive functioning.

We designed a refined replication of the Jelicic and co-workers experiment [7] to evaluate the possibility of learning during nitrous oxide/oxygen/enflurane anaesthesia in spontaneously breathing patients. The design also permitted an investigation of the activation paradigm.

Patients and methods

Patients
Fifty-two female patients (ASA I or II) scheduled for body surface surgery under standardized general anaesthesia at the Western Infirmary in Glasgow were invited to take part in the study, which was approved by the local medical ethics committee. Patients with hearing problems, intellectual impairments, and neurologic or psychiatric disorders were excluded.

Procedure
The patients were randomly assigned to two groups, and the study was conducted in a double-blind fashion. On the afternoon before surgery preoperative anxiety was assessed using the state version of the State-Trait Anxiety Inventory [9]. Immediately after first incision by the surgeon the patients were played an audio tape at a normal, but relatively loud listening volume. For all the patients, the tape contained 5 min of natural seaside sounds (as a filler sound) followed by ten repeated recordings over 15 min. For group A the recording comprised 10 common facts of several years ago (e.g., "Dr. Beeching cut the size of British Railways"). A pilot study in a comparable sample of patients had shown that these facts were largely forgotten. For group B the recording contained 20 fictitious—i.e., nonfamous—names (e.g., "Daniel Murray," "Hilary Kline," and "John Dolan"). Each recording lasted for about 90 sec. Twenty min after first incision the first tape was replaced by a second one containing only seaside sounds, played for the remainder of the operation.

Anaesthesia
Morphine 10-15 mg and cyclizine 50 mg were administered by i.m. injection 45 min before operation. After the insertion of a cannula to the dorsum of the patient's hand, anaesthesia was induced with i.v. thiopentone, sufficient to abolish the eyelash reflex, and maintained with nitrous oxide and enflurane in 34% oxygen. A laryngeal mask was inserted, and all patients breathed spontaneously throughout (Mapleson A system). The inspired concentration of enflurane was altered as required to provide optimum surgical conditions.

Systolic, diastolic and mean arterial pressures were recorded at 5 min intervals using a non-invasive blood pressure monitor throughout the surgical procedure; heart rate, electrocardiograph, inspired oxygen concentration and end-tidal (ET) oxygen, carbon dioxide and enflurane concentrations were monitored continuously; continuous oxygen saturation measurements were made using an oximeter probe placed on the patient's finger. Patients undergoing mastectomy received an i.v. infusion of Hartmann's solution.

After the completion of surgery, the patients were admitted to the Recovery Room, and after a period of routine management returned to the same surgical ward. Postoperative analgesia, morphine 10 mg and cyclizine 50 mg was administered when required.

Interview and tests
The postoperative interview took place on the morning after the surgical procedure. The patients were first asked about any conscious awareness during anaesthesia using the following three questions: "What is the last thing you remember before you were put asleep for your operation?", "What is the first thing you remember after your operation?", and "Do you remember anything between?" Next, the patients were given 15 questions about past events. Ten of these questions related to the statements presented intraoperatively to group A (e.g., "Which politician reduced the size of British Railways?"). Implicit memory by activation of pre-existing memory representations would be indicated if patients from group A answered

more of these ten questions correctly than patients in group B. Finally, the patients were asked to state whether each of 30 combinations of first names and surnames belonged to a famous person or not. Ten of these names corresponded to names played to group B while anaesthetized (e.g., Daniel Murray), ten other names contained parts (five of them shared the first name, five others the surname) of the intraoperatively presented names (e.g., Hilary Richman, Brian Dolan), and the remaining ten names were filler names (five of these were moderately famous, e.g., Delia Smith).

The conceptual basis of this test is that nonfamous names presented during anaesthesia would lead to increased perceived familiarity of these names after the operation. Since the patients would not know that the names had been presented intraoperatively, they would interpret the sense of familiarity as indicating that the name had some degree of fame (the test was validated by Jacoby and co-workers [10,11]). Implicit memory for new associations (true learning) would be expressed if patients in group B, compared with those from group A, designated more fame to unique combinations of names (which lack by definition any pre-existing memory representation), but not to names of which only first names or surnames were played during anaesthesia. If group B also attributed more false fame to names that were partly presented than group A, then activation of old knowledge would probably be involved (see [6] for a discussion of this issue).

Data analysis

Data were analysed with Student's t-tests to detect differences between groups. A probability value of less than 0.05 was considered statistically significant.

Results

Six patients refused to take part in the experiment; three were excluded because they received a benzodiazepine premedication; one patient dropped out because her surgical procedure took less than 20 minutes and one because she was ASA III and required a different anaesthetic technique. Hence, 41 patients were enrolled in the study (mean age 54 yr, range 27-76). The majority of the patients underwent breast surgery (e.g., breast biopsy, lumpectomy or mastectomy). Group A consisted of 20 patients, Group B of 21 patients. The mean ET enflurane concentration, during the period in which the experimental stimuli were administered, was 1.1% (range 0.6-1.9%). There were no significant differences between the two groups with respect to age, number of previous operations, preoperative anxiety, duration of anaesthesia, duration of surgery, and ET-concentrations of enflurane (all p-values > 0.25).

None of the patients had conscious recall of any intraoperative events. Neither implicit memory test produced evidence for information-processing during anaesthesia. Mean (SEM) number of correct answers on the common facts test was 4.55 (0.63) for group A, and 4.0 (0.59) for group B ($t = 0.63$, $df = 39$, $p = 0.53$). Mean (SEM) number of the 10 nonfamous names that were designated as famous on the learning test was 1.24 (0.36) for group B, and 1.3 (0.26) for group A ($t = 0.14$, $df = 39$, $p = 0.89$). In addition, compared with group A, group B did not attribute more fame to the ten nonfamous names with only first names or surnames presented during anaesthesia (p equals 0.22 and 0.61, respectively). Neither for the five filler questions from the common facts test, nor for the nonfamous filler names from the famous names test, was there a difference between groups (p-values > 0.50).

Discussion

We failed to find an implicit memory effect with nitrous oxide/oxygen and enflurane (in spontaneously breathing patients) whereas unconscious learning and activation during anaesthesia were demonstrated in our previous study [7] with nitrous oxide/oxygen and alfentanil (in ventilated patients).

Apart from these changes in anaesthetic technique, the two studies differ in time lapse between presentation of stimuli and postoperative testing. Patients in the previous study were interviewed 2-3 hours after the surgical procedure, while we did not test our patients until the following morning (most of our patients underwent intermediate instead of minor surgery). However, it seems unlikely that our null findings are solely due to a longer time interval before testing. Block, Ghoneim, Sum Ping and Ali [3], for instance, found evidence for intra-anaesthetic cognitive processing—with implicit memory tests—on the day after surgery, and long lasting implicit memory effects have also been reported in patients with organic amnesia [12,13].

The anaesthetic technique used in our study may largely account for the failure to demonstrate learning or activation during anaesthesia. Thornton and colleagues [14] have studied the auditory evoked response (AER) in patients anaesthetized with nitrous oxide/oxygen and enflurane. They found a dose-related effect of enflurane on the brainstem and early cortical components of the AER and reported that the waves originating from the thalamus and primary auditory cortex were almost abolished at an ET-concentration of 1.22%. In our study, the mean ET enflurane concentration—during the period in which the experimental stimuli were administered—was 1.1%. Given the results of the AER study above, this might imply a largely reduced transmission of auditory signals to the cerebral cortex in our patients. Interestingly, Jansen, Bonke, Klein, van Dasselaar, and Hop [15] recently failed to demonstrate unconscious perception during enflurane anaesthesia using postoperative motor responses.

To make matters more complex, Roorda-Hrdličková, Wolters, Bonke, and Phaf [1] and Block and co-workers [3] found evidence for activation of old, pre-existing knowledge during anaesthesia with a volatile anaesthetic, i.e., isoflurane. How is one to explain the discrepancy between the latter findings and our own? In the studies with positive results the patients were paralysed and mechanically ventilated, whereas in our study patients were not given muscle relaxants and breathed spontaneously. It is possible that Roorda-Hrdlicková and colleagues [1] and Block and associates [3] were able to demonstrate information-processing because the experimental stimuli were presented during a brief lightening in the state of anaesthesia [16]. Such temporarily lightened stages of anaesthesia are less likely to occur in patients without neuromuscular blockade: spontaneous movements in awakening patients would make anaesthetists aware of this happening and make surgery impossible.

References

1. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 150-155.

2. Jelicic M, Bonke B, Appelboom DK. Indirect memory for words presented during anaesthesia. *Lancet* 1990; *ii:* 249.

3. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Human learning during general anaesthesia and surgery. *British Journal of Anaesthesia* 1991; *66:* 170-178.

4. Richardson-Klavehn A, Bjork RA. Measures of memory. *Annual Review of Psychology* 1988; *39:* 475-543.

5. Millar K. The assessment of memory for anaesthesia. In: Hindmarch I, Jones JG, Moss E, eds. *Aspects of Recovery from Anaesthesia.* London: Wiley, 1987: 75-91.

6. Kihlstrom JF, Schacter DL. Anaesthesia, amnesia, and the cognitive unconscious. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 21-44.

7. Jelicic M, De Roode A, Bovill JG, Bonke B. Unconscious learning during anaesthesia. *Anaesthesia,* in press.

8. Utting JE. Clinical aspects of awareness during anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 259-271.

9. Spielberger CD, Gorsuch RL, Lushene RE. *Manual of the State-Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press, 1970.

10. Jacoby LL, Kelley CM. Unconscious influences of memory for a prior event. *Personality and Social Psychology Bulletin* 1987; *13:* 314-336.

11. Jacoby LL, Woloshyn V, Kelley CM. Becoming famous without being recognized: Unconscious influences of memory produced by dividing attention. *Journal of Experimental Psychology* (General) 1989; *118:* 115-125.

12. McAndrews MP, Glisky EL, Schacter DL. When priming persists: long lasting implicit memory for a single episode in amnestic patients. *Neuropsychologia* 1987; *25:* 497-506.

13. Backer Cave C, Squire LR. Intact and long-lasting repetition priming in amnesia. *Journal of Experimental Psychology* (Learning, Memory, Cognition) 1992; *18:* 509-520.

14. Thornton C, Catley DM, Jordan C, Lehane JR, Royston D, Jones JG. Enflurane anaesthesia causes graded changes in the brainstem and early cortical auditory evoked response in man. *British Journal of Anaesthesia* 1983; *55:* 479-485.

15. Jansen CK, Bonke B, Klein J, van Dasselaar N, Hop WCJ. Failure to demonstrate unconscious perception during balanced anaesthesia by postoperative motor response. *Acta Anaesthesiologica Scandinavica* 1991, *35:* 407-410.

16. Millar K. Recall, recognition and implicit memory for intra-anaesthetic events. *Ballière's Clinical Anaesthesiology* 1989, *3:* 487-510.

Chapter 9

General discussion

This final chapter contains an evaluation of the studies presented in the previous four chapters, followed by practical implications, and suggestions for future research into information-processing under general anaesthesia.

Chapter 5 described an experiment designed to investigate the effect of different intra-anaesthetic therapeutic suggestions on postoperative well-being in cholecystectomy patients. We hypothesized that patients administered affirmative positive suggestions would show a more favourable course than those exposed to either a mixture of affirmative and nonaffirmative suggestions, nonaffirmative suggestions only, or an irrelevant story. Contrary to our expectations, patients who had been played mixed suggestions spent less time in hospital than those in the other groups. This suggests that intraoperative suggestions accelerate postoperative recovery only when they contain both affirmative and nonaffirmative suggestions.

It is difficult to explain the reduction in hospital stay after mixed suggestions. Why should affirmative and nonaffirmative statements together be more effective than affirmative ones alone? There is a possibility that—although we applied a correction for type I error—our positive result is due to chance. Liu and colleagues recently pointed out that—given the many factors which influence the decision to discharge patients—duration of hospital stay is a rather insensitive index of recovery from surgery [1]. In addition, we did not find any differences between the groups with respect to postoperative subjective well-being. Moreover, two recent investigations have failed to find any effect of therapeutic messages on postoperative course [1,2]. Our results could therefore be interpreted as a null-finding. However, other studies have yielded evidence for an improved and faster recovery after intraoperative suggestions [3-5]. Future research will probably shed more light on the efficacy of different forms of verbal suggestions during anaesthesia.

What can be said about the psychodynamic mechanisms of intra-anaesthetic therapeutic suggestions (see Chapter 4)? Not very much. Given the limited information-processing capabilities of anaesthetized patients [6], it would be unlikely that "secondary process thinking" occurs whilst under anaesthesia [7]. However, "primary process thinking" may still be active during this state of pharmacological unconsciousness.

Studies of therapeutic suggestions during anaesthesia are sometimes difficult to interpret. In the case of a null-finding it remains unclear whether or not stimulus registration has occurred under anaesthesia. One could then argue that no cognitive processing has taken place during this state of induced unconsciousness. On the other hand, it is also possible that the suggestions were indeed registered by the anaesthetized cortex, but that patients were unable or unwilling to respond to them.

Activation of old, pre-existing knowledge during anaesthesia was convincingly demonstrated in an implicit memory study by Roorda-Hrdličková and co-workers [8]. Chapter 6 contains a successful replication of their investigation using a different anaesthetic technique. During anaesthesia, experimental patients were presented with two target words from each of two semantic categories. Patients in the control group were played neutral sounds. In the immediate postoperative period, the patients were asked to generate examples of the two categories. Patients in the experimental group produced significantly more target words than control patients.

Neuropsychological research employing implicit memory paradigms has shown that patients with organic amnesic syndromes are able to form new associations in memory [9,10].

Such new learning might also occur during anaesthesia. Chapter 7 therefore presents an experiment conducted to investigate the underlying mechanisms of memory in anaesthesia. Are anaesthetized patients capable of learning novel information or are their cognitive processing functions limited to activation of old, pre-existing knowledge? This study also permitted a replication of the activation paradigm. Whilst anaesthetized, patients were either played common facts of some years ago (group A: "Activation") or a list of fictitious (nonfamous) people (group B: "Learning"). Postoperatively, patients were given two implicit memory tests. Patients in group A were better able to answers questions about the experimental common facts than those from group B, whereas the latter group designated more experimental fictitious names as famous than the former. This finding suggests that these nonfamous names—which probably lack any pre-existing memory representation—gained in familiarity as a result of a new memory trace. Since the patients were not aware of having heard these names during anaesthesia, they had no other choice than to attribute the familiarity of the names to "fame" rather than intraoperative presentation. Apparently, information-processing under anaesthesia can also take place as new learning (a more sophisticated form of cognitive functioning than activation).

In Chapter 8 an unsuccessful replication of the latter study with different anaesthetic agents was reported. Using the same paradigm as in Chapter 7, we found no evidence for either activation of old knowledge or new learning during enflurane anaesthesia.

It seems that cognitive processing and memory storage in anaesthetized patients is possible under certain conditions. The best evidence for this hypothesis comes from implicit memory studies. However, it is not clear which factors are involved in memory under anaesthesia. Evidently, the anaesthetic cocktail is of importance. Jones and Konieczko pointed out that different anaesthetics have different effects on the central nervous system [11]. They reported that cerebral auditory pathways are more depressed by volatile agents than by intravenous anaesthetics. Hence, the possibility of stimulus registration would be less likely under inhalation anaesthesia. We were able to demonstrate implicit memory effects with nitrous oxide/oxygen/opioid techniques but not with enflurane anaesthesia. In addition, Bonke and co-workers failed to find evidence for implicit memory during halothane anaesthesia in children [12]. However, investigations by Roorda-Hrdličková and colleagues [8], Kihlstrom and his group [13], and Block and associates [14] did produce evidence for activation during isoflurane anaesthesia. Furthermore, other (psychological) factors may also be determinants of information-processing and memory storage under anaesthesia. Goldmann [15] argued that salience of the message, patients' motivation, and the postoperative testing situation are likely to influence intraoperative perception. Finally, some classes of implicit memory tests seem to be more useful, or sensitive, in detecting intraoperative unconscious perception than others (cf. Roediger's distinction between perceptual and conceptual implicit memory tests [16,17]).

What are the practical implications of memory during anaesthesia? As was noted in Chapter 1, "negatively coloured" statements, made during surgery, about the unconscious patient, may have a harmful effect on postoperative well-being. Unfortunately, most of the material supporting this contention is anecdotal in nature (see [7] for a review). However, if implicit memory occurs during anaesthesia, then some retention of unfavourable comments is to be expected [18]. Some authors believe it is necessary to caution anaesthetists, nurses, and surgeons to exercise restraint in their conversation in the operating theatre and assume that some of these conversations may be retained by the anaesthetized patient [19]. Others have argued that patients should be provided with earplugs while under anaesthesia [20,21] or have suggested that recordings of therapeutic suggestions or relaxing music be played to unconscious patients [22,23]. It might indeed be helpful to play music to patients undergoing "light levels of anaesthesia" (e.g., during cardiovascular procedures). This may prevent psychological trauma due to the patient overhearing intraoperative conversation.

Given the many problems associated with investigations which used postoperative motor responses or therapeutic suggestions, it would be best to study cognitive processing in anaesthetized patients with implicit memory paradigms [24]. Although several implicit memory tests have already proved to be of some use in detecting activation or learning during anaesthesia [8,13,14], it would be important to determine which type of tests yields the most reliable evidence for intraoperative stimulus registration. Replication of published studies is therefore necessary. The most sensitive tests could then be used to investigate unconscious perception with different anaesthetic cocktails and/or dosages. Such research may provide the anaesthesiologist with (safe) anaesthetic techniques that prevent implicit memory storage [11].

From a more psychological point of view, it would be interesting to investigate whether or not an implicit memory effect occurs if patients are objectively unaware of stimuli presented during anaesthesia. It is questionable whether or not—in studies of memory in anaesthesia—all patients were unconscious during presentation of the experimental stimuli [25]. At present, however, there is no reliable and objective indicator of the anaesthetic state available (although auditory evoked potentials in the E.E.G. could possibly be a reliable monitor of "depth of anaesthesia") [26]. Very recently, Merikle and Rondi [27] described alternative research paradigms which could "filter out" any semi-conscious information-processing in anaesthetized patients. These paradigms are likely to produce valuable data about the nature of unconscious auditory perception during general anaesthesia.

References

1. Liu WHD, Standen PJ, Aitkenhead AR. Therapeutic suggestions during general anaesthesia in patients undergoing hysterectomy. *British Journal of Anaesthesia* 1992; *68:* 277-281.

2. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Efficacy of therapeutic suggestions for improved postoperative recovery presented during general anesthesia. *Anesthesiology* 1991; *75:* 746-755.

3. Bonke B, Schmitz PIM, Verhage F, Zwaveling A. Clinical study of so-called unconscious perception during general anaesthesia. *British Journal of Anaesthesia* 1986; *58:* 957-964.

4. Evans C, Richardson PH. Improved recovery and reduced postoperative stay after therapeutic suggestions during general anaesthesia. *Lancet* 1988; *ii:* 491-493.

5. McLintock TTC, Aitken H, Downie CFA, Kenny GNC. Postoperative requirements in patients exposed to intraoperative suggestions. *British Medical Journal* 1990; *301:* 788-790.

6. Kihlstrom JF, Schacter DL. Anaesthesia, amnesia, and the cognitive unconscious. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 21-44.

7. Bonke B. Psychological consequences of so-called unconscious perception and awareness in anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 197-218.

8. Roorda-Hrdličková V, Wolters G, Bonke B, Phaf RH. Unconscious perception during general anaesthesia, demonstrated by an implicit memory task. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 150-155.

9. Moscovitch M, Winocur G, McLachlan D. Memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal Of Experimental Psychology* (General) 1986; *115:* 331-347.

10. Gordon B. Preserved learning of novel information in amnesia: Evidence for multiple memory systems. *Brain and Cognition* 1988; *7:* 257-282.

11. Jones JG, Konieczko K. Hearing and memory in anaesthetised patients. *British Medical Journal* 1986; *292:* 1291-1293.

12. Bonke B, Van Dam ME, Van Kleef JW, Slijper FME. Implicit memory tested in children with inhalation anaesthesia. *Anaesthesia,* in press.

13. Kihlstrom JF, Schacter DL, Cork RC, Hurt A, Behr SE. Implicit and explicit memory following surgical anesthesia. *Psychological Science* 1990; *1:* 303-306.

14. Block RI, Ghoneim MM, Sum Ping ST, Ali MA. Human learning during general anaesthesia and surgery. *British Journal of Anaesthesia* 1991; *66:* 170-178.

15. Goldmann L. Factors determining the probability of recollection of intraoperative events. In: Bonke B, Fitch W, Millar, K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 45-49.

16. Roediger HL III. Implicit memory. Retention without remembering. *American Psychologist* 1990; *45:* 1043-1056.

17. Tulving E. Varieties of consciousness and levels of awareness in memory. In: Baddeley A, Weiskrantz L, eds. *Attention: Selection, Awareness and Control. A tribute to Donald Broadbent.* Oxford: Oxford University Press, in press.

18. Goldmann L. Information-processing under general anaesthesia: A review. *Journal of the Royal Society of Medicine* 1988; *81:* 224-227.

19. Ghoneim MM, Block RI. Learning and consciousness during general anesthesia. *Anesthesiology* 1992; *76:* 279-305.

20. Anonymous. Advertising during anaesthesia (editorial). *Lancet* 1986; *ii:* 1019-1020.

21. Davis R. Anaesthesia, amnesia, dreams and awareness. *Medical Journal of Australia* 1987; *146:* 4-5.

22. Evans C, Richardson PH. A double-blind randomized placebo-controlled study of therapeutic suggestions during general anaesthesia. In: Bonke B, Fitch W, Millar K, eds. *Memory and Awareness in Anaesthesia.* Amsterdam: Swets & Zeitlinger, 1990: 120-130.

23. Korunka C, Guttmann G, Schleinitz D, Hilpert M, Haas R, Fitzal S. Music and positive suggestions presented during general anaesthesia—effects on analgesic consumption and postoperative well-being. In: Sebel PS, Winograd E, Bonke B, eds. *Memory and Awareness in Anesthesia: Second International Symposium.* In press.

24. Millar K. The inconsistent findings of studies of memory for intraoperative events. In: Sebel PS, Fitch W, eds. *Monitoring the Central Nervous System.* Baltimore: Williams & Wilkins, in press.

25. Millar K. Recall, recognition and implicit memory for intra-anaesthetic events. *Ballière's Clinical Anaesthesiology* 1989; *3:* 487-510.

26. Jones JG. Depth of anaesthesia and awareness. In: Nunn JF, Utting JE, Brown BR Jr, eds. *General Anaesthesia.* London: Butterworths, 1989: 419-427.

27. Merikle PM, Rondi G. Memory for events during anesthesia has not been demonstrated: A psychologist's viewpoint. In: Sebel PS, Winograd E, Bonke B, eds. *Memory and Awareness in Anaesthesia: Second International Symposium.* In press.

Samenvatting

In dit proefschrift wordt onderzocht of onbewuste auditieve informatie-verwerking kan plaatsvinden onder algehele anesthesie. Hoofdstuk 1 beschrijft hoe het incidenteel kan gebeuren dat patiënten te weinig anesthesie ontvangen en bij bewustzijn komen tijdens de operatie. Een fenomeen dat bekend staat als "awareness" onder anesthesie. Bovendien worden in dit hoofdstuk gevalsbeschrijvingen vermeld die suggereren dat ook tijdens adequate anesthesie—op een onbewuste wijze—geluiden kunnen worden waargenomen. Hoofdstuk 2 geeft een selectief overzicht van experimenteel-psychologisch onderzoek naar onbewuste processen. Drie researchgebieden worden beschreven: subliminale waarneming, onbewuste interne verwerkingsalgoritmen en impliciet geheugen. Geconcludeerd wordt dat veel cognitieve processen buiten het bewustzijn om plaatsvinden. In hoofdstuk 3 wordt de literatuur op het gebied van de stimulus registratie tijdens anesthesie besproken. Vier onderzoeksmethoden komen aan de orde: hypnose, postoperatieve motorische responsen, therapeutische suggesties en impliciete geheugentests. Onderzoeken waarbij gebruik is gemaakt van therapeutische suggesties of impliciete geheugentests lijken evidentie voor intraoperatieve waarneming van geluiden te leveren. Hoofdstuk 4 gaat in op de achtergronden van de empirische studies die in het proefschrift worden beschreven. Hoofdstuk 5 bevat een onderzoek naar het effect van verschillende therapeutische suggesties tijdens anesthesie op het postoperatieve beloop van cholecystectomie-patiënten. Uit dit experiment blijkt dat patiënten die zowel positieve als ontkende negatieve therapeutische suggesties aangeboden hadden gekregen eerder uit het ziekenhuis werden ontslagen dan degenen die alleen positieve respectievelijk ontkende negatieve suggesties of een irrelevant verhaal te horen hadden gekregen. In de volgende drie hoofdstukken worden studies met impliciete geheugentests beschreven. Hoofdstuk 6 laat zien dat bestaande kennis kan worden geactiveerd tijdens anesthesie, terwijl hoofdstuk 7 evidentie levert voor nieuw leren—naast activatie—in patiënten onder anesthesie. In hoofdstuk 8 wordt een onderzoek beschreven (met een verschillende anesthesie-techniek) waarin geen informatie-verwerking tijdens anesthesie kon worden aangetoond. Hoofdstuk 9 bevat een evaluatie van de empirische studies uit het proefschrift. Geconcludeerd wordt dat—gegeven bepaalde omstandigheden—onbewuste waarneming van geluiden kan plaatsvinden tijdens algehele anesthesie. Daarnaast worden praktische implicaties van intraoperatieve stimulusregistratie besproken. Het hoofdstuk wordt afgesloten met enkele suggesties voor toekomstig onderzoek.

Summary

This thesis describes experimental investigations to determine whether unconscious auditory information-processing can occur under general anaesthesia. Chapter 1 explains how patients may incidentally receive inadequate anaesthesia and regain consciousness during surgery: A phenomenon which is also known as "awareness" in anaesthesia. In addition, the chapter mentions case-studies which suggest that unconscious perception of sounds can take place during adequate anaesthesia. Chapter 2 provides a selective review of experimental psychological research into unconscious processes. Three research areas are described: subliminal perception, internal processing algorithms and implicit memory. It is concluded that many cognitive processes occur without awareness. In Chapter 3, the literature on stimulus registration during anaesthesia is reviewed. Three research-strategies are discussed: hypnosis, postoperative motor responses, therapeutic suggestions, and implicit memory tests. Studies which used therapeutic suggestions or implicit memory tests seem to produce evidence for intraoperative perception of sounds. Chapter 4 provides the background for the empirical investigations of the thesis. Chapter 5 contains a study of the effects of different therapeutic suggestions during anaesthesia on the postoperative course of cholecystectomy patients. The experiment shows that patients who were presented with affirmative and nonaffirmative suggestions were discharged from hospital more quickly than those exposed seperately to affirmative or nonaffirmative suggestions, or an irrelevant story. The next three chapters describe studies which employed implicit memory tests. Chapter 6 shows that old, pre-existing knowledge can be activated during anaesthesia, whereas the Chapter 7 produces evidence for new learning in anaesthetized patients (in addition to such activation). In Chapter 8 an experiment is described (with a different technique of anaesthesia) in which no evidence for information-processing under anaesthesia was found. The final chapter contains an evaluation of the empirical investigations reported in the thesis. It is concluded that, under certain conditions, unconscious perception of sounds can occur during general anaesthesia. Some practical implications of intraoperative stimulus registration are also discussed. The chapter ends with suggestions for future research in this area.

Acknowledgments

I wish to thank the following persons or institutions:

- My supervisor and "co-promotor" Dr. Benno Bonke who helped me with almost every aspect of my doctoral research, i.e. research design, data analysis, data interpretation, conclusions, etc. and made useful suggestions to improve the text of my dissertation.

- My "promotor" Prof.dr. Frans Verhage for valuable comments on the manuscript.

- Prof. Keith Millar who helped me with the study described in Chapter 8, gave me the opportunity to finish my thesis at the Behavioural Sciences Group of Glasgow University, and was a member of "de kleine commissie."

- Prof.dr. H. Collewijn for his willingness to take part in "de kleine commissie" and for his helpful comments on the text.

- Dr. J.H. Keeman who made the investigations in St. Lucas Hospital, Amsterdam, possible. The Departments of Anaesthesiology, General Surgery and Plastic Surgery at St. Lucas Hospital for their cooperation and hospitality.

- Dr. Gezinus Wolters and Dr. Hans Phaf who co-authored Chapter 6.

- Dr. Annemiek de Roode and Prof. dr. J.G. Bovill for their cooperation in the experiment described in Chapter 7. The Department of Ophthalmic Surgery at the University Hospital Leiden for their help and hospitality.

- Dr. John Asbury who helped me with the research described in Chapter 8. Dr. K.M.S. Dewar and Prof. D. George for their advice and for allowing me to study the patients under their care at the Western Infirmary Glasgow.

- The British Council (Amsterdam) and Stichting Universiteitsfonds Rotterdam for the financial support that made my research work in Glasgow possible.

- All 216 Dutch and British surgical patients who volunteered to participate in the experiments.

- My colleagues from the Department of Medical Psychology and Psychotherapy of Erasmus University and the Behavioural Sciences Group of Glasgow University for their advice and support.

- Drs. Frank van der Velde who helped with the lay-out of my dissertation.

Curriculum vitae

Marko Jelicic was born on 12 January 1959 in Amersham (England). After secondary school he qualified as a laboratory technician and worked as such for two years. He subsequently studied psychology at the University of Amsterdam from 1982 to 1987 and graduated in experimental and physiological psychology. He worked as a research assistant ("assistent in opleiding") in the Department of Medical Psychology and Psychotherapy of Erasmus University Rotterdam from 1988 to April 1992. During the first six months of 1992 he was a visiting researcher to the Behavioural Sciences Group of Glasgow University (Scotland).