Processing Familiar and Unfamiliar Auditory Stimuli During General Anesthesia

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We tested memory priming for auditory stimuli presented during general propofol-sufentanil anesthesia in 58 patients undergoing day-case arthroscopic surgery. Stimuli were presented via headphones and consisted of common facts (Group A, 29 patients), or familiar and unfamiliar full names of fictitious people (Group B, 29 patients). Group A was expected to give more correct answers to questions about the common facts than Group B, when tested postoperatively, and Group B to attribute more fame to presented names than Group A (famous names test). Because the process for learning new or unfamiliar stimuli (elaboration) in particular may be impaired under general anesthesia, more memory priming was expected for familiar than for unfamiliar material. No significant differences were demonstrated between the two groups in performance on common facts or in fame attributed to the names. The amount of memory priming, however, was positively related to one of two measures of preoperative anxiety.

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Implicit memory during general anesthesia (GA) (1) may reflect brief moments of conscious information processing (2) or some simple form of (nonconscious) learning. Intact implicit-memory performance without conscious recollection is also seen in anterograde amnesia (3) and in normal subjects (4,5). Finding similar qualitative differences (6) would suggest that some form of learning is common during anesthesia, without necessarily indicating awareness.

Only low-level information processing is considered possible during nonconscious states (7), including that induced by GA (8–12). One form of low-level processing is activation learning (13–16) (i.e., activation and strengthening of existing memory representations). Elaboration learning (i.e., creating new representations in memory), which may be impaired in nonconscious states, is considered a prerequisite for conscious recall. Nonetheless, implicit memory performance for seemingly new verbal associations was found recently (17). Full (i.e., first and last) names of fictitious people were presented during GA. Postoperatively, patients rated whether a name belonged to a famous person. Unaware that some names had been presented intraoperatively, patients would interpret any sense of familiarity as indicating that the name had some degree of fame (18). The full names may have been new for most patients, but not the first and last names themselves. Implicit memory performance may, therefore, merely have reflected the activation of either name [but see also Jelicic et al. (19) and De Roode et al. (20)].

We tested, in a modified replication, whether information processing during anesthesia is restricted to activation learning. We manipulated the novelty of stimuli for the "names test" by using familiar, and quite unfamiliar, names, assuming that more elaboration is required for storing unfamiliar names than for familiar names. Thus the larger implicit-memory effect was expected for familiar names, in contrast with what is usually found during consciousness (21).

We also used the common-facts test, based on the notion that largely forgotten facts are reactivated when presented during anesthesia. This may, by activation learning alone, lead to more correct answers to relevant questions in patients presented with the facts than in a control group.

Methods

Forty-two male and 21 female patients (mean age 40 yr; ASA grade I; day-case arthroscopic surgery under GA) consented to participate in the study, which was approved by the local medical ethics committee.

Variation between patients was eliminated as much as possible in a routine clinical set-up by using only

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one kind of surgical operation of comparable duration, performed at the same time of day, with a standardized anesthetic technique, all given by one anesthesiologist (TP). We used an anesthetic mixture containing sufentanil 0.45 μg and propofol 9.1 mg/mL, i.e., 1 mL sufentanil (5 μg/mL) per 10 mL propofol (10 mg/mL), administered by a syringe pump (Graseby 3400; Graseby Medical Ltd., Watford, Herts, UK). Induction dose was calculated as 0.2 mL/kg body weight (BW) and maintenance dose as 15 mL + 0.2 mL/kg BW. Actual BW was corrected in patients who 1) smoked more than nine cigarettes daily, 2) drank more than two alcoholic beverages daily or >21 a week, 3) were considered anxious, or 4) were used to doing physical exercises at least three times a week for >1 h, by scaling it 10 kg higher; in patients over 60 yr old BW was corrected by scaling it 10 kg lower. No premedication was given. Induction started with intravenous boluses of atropine 0.5 mg and sufentanil 15 μg, followed by a fast infusion (1200 mL/h) of the anesthetic mixture until the calculated induction dose was reached. Then we changed the infusion to the calculated maintenance rate. After disappearance of the eyelash reflex, partial paralysis was obtained by an intravenous bolus of atracurium, 15 mg for the laryngeal mask and 25 mg in case of intubation. The lungs were mechanically ventilated (air/oxygen) to obtain P_{ETCO_2} of 35 ± 2 mm Hg. If anesthesia was considered too light (limb movement, increase in blood pressure and/or heart rate > 10%), a bolus of 2 mL mixture was given and infusion rate increased by 2 mL/h. If it was considered too deep (blood pressure >25% below preoperative value, heart rate < 50 bpm), the infusion rate was decreased by 2 mL/h.

Patients were assigned randomly to Groups A and B (subdivided into B1 and B2, see below) in a double-blind fashion. Independent variables were "type of stimuli" (common facts or names) and "familiarity of names." Dependent variables were scores on the names test and the common-facts test. Data were analyzed by analysis of variance.

Based on a pilot study, 10 mostly forgotten facts were chosen as stimuli for Group A; for Group B, 10 familiar and 10 unfamiliar full names were selected. Two lists (1 and 2) of 10 names were created, with an equal number of familiar and unfamiliar names and of female and male names. List 1 was presented intraoperatively to Subgroup B1 and List 2 to Subgroup B2. Eight tapes were prepared. Four contained the 10 common facts, two contained List 1, and two List 2, all randomly ordered. Common facts and lists of names were presented 10 times, followed by filler sound, using a tape recorder and headphones. The experimenter was unaware of which tape was played to a patient.

Postoperatively, common facts were tested with a list of 20 questions, 10 concerning the facts presented to Group A and 10 new questions. The names test was a list of the 20 experimental names (Lists 1 and 2) and 10 new names. Patients rated each name on a 65-mm visual analog scale, with anchors "not at all famous" and "famous."

On the day of surgery, preoperative anxiety was assessed with the State-Trait Anxiety Inventory (22) and the Hospital Anxiety and Depression Scale (23). Immediately after the first incision the appropriate tape was played, starting with 5 min of filler sound to allow adjustment of anesthesia if necessary.

Patients were interviewed 15 min after they were wide awake, i.e., 30–60 min postoperatively. Conscious recall of events during anesthesia was probed using standard questions. Then patients rated the fame of the names, read out by the experimenter, and answered the 20 common-facts questions.

Results

Four patients were excluded because their operations took less than the duration of the experimental tape, one because benzodiazepines had been administered preoperatively. Results of 40 males and 18 females (n = 29 for both Groups A and B) were analyzed. No differences in relevant variables were found between intubated patients (n = 10) and those with a laryngeal mask (n = 48). Therefore, these groups were merged. Groups A, B1, and B2, did not differ in age, preoperative anxiety, or duration of surgery (Table 1). No differences between Groups A and B were found for the 10 nonpresented questions in the common-facts test ($F(1,56) = 0.002$, not significant [NS]) nor for the 10 filler names in the names test ($F(1,56) = 1.15$, NS) (Table 2). There was, however, a difference for the 10 filler names between Subgroups B1 (39.08) and B2 (30.55) ($F(1,28) = 4.30$, $P < 0.05$). Therefore, Subgroups B1 and B2 were analyzed separately.

There was no conscious recall whatsoever. Mean numbers of correct common facts in Groups A (2.93) and B (2.72) did not differ significantly ($F(1,56) = 0.14$, NS), nor did mean scores on the names test (A 5.96 vs B 7.66) ($F(1,56) = 1.11$, NS). Mean (SD) scores on the names test for the two subgroups and for the two categories of names (familiar and unfamiliar) are presented in Table 3. As expected, the overall mean score for all familiar names (8.33) was higher than for unfamiliar names (5.28) ($F(1,56) = 15.87$, $P < 0.0005$). In absolute terms, priming was larger for familiar names than for unfamiliar names, but not significantly so ($F(1,56) = 0.93$, NS).

On a *post-hoc* basis, standard normal scores for memory priming were determined by taking the difference between patients' scores on their experimental stimuli and the mean score for these stimuli in patients

Table 1. Distribution of Scores on Descriptive Variables for Groups A and B, and for Subgroups B1 and B2

	Group A (n = 29)	Group B (n = 29)	Subgroup B1 (n = 16)	Subgroup B2 (n = 13)
M/F	17/12	23/6	13/3	10/3
Age (yr)	39.9 (10.0)	38.3 (10.9)	39.0 (9.5)	37.4 (12.8)
HAD-A	3.6 (2.4)	4.0 (2.7)	3.8 (2.7)	4.3 (2.8)
STAI-state	36.7 (11.0)	37.9 (10.9)	36.8 (11.5)	39.2 (10.3)
Duration	27.6 (9.0)	28.6 (12.2)	26.4 (11.5)	31.2 (12.9)

Values are mean (SD) for continuous variables.
M/F = male/female ratio; Duration = duration of anesthesia in minutes; HAD-A = Hospital Anxiety and Depression Scale, anxiety score; STAI-state = state version of the State-Trait Anxiety Inventory.

Table 2. Number of Correct Answers on the Common-Facts Test and on the Names Test

	Group A	Group B	Subgroup B1	Subgroup B2
Common facts[a]				
Experimental	2.93 (1.7)	2.72 (2.5)	2.94 (2.6)	2.46 (2.4)
Nonpresented	5.45 (2.9)	5.32 (3.0)	5.94 (2.9)	4.77 (3.0)
Names[b]				
Experimental	5.96 (5.6)	7.66 (8.1)	7.03 (7.8)	8.43 (8.4)
Famous fillers	32.18 (10.2)	35.26 (11.6)	39.08* (11.1)	30.55* (10.9)

[a] Values are mean (SD).
[b] Values are mean (SD) in millimeters; names were rated on a 65-mm visual analog scale where higher scores indicated more fame attributed to the name.
* P(diff) < 0.05.

Table 3. Scores on the Names Test for Familiar and Unfamiliar Names Separately

	List 1		List 2	
	Subgroup B1 (n = 16)	Group A + Subgroup B2 (n = 42)	Subgroup B2 (n = 13)	Group A + Subgroup B1 (n = 45)
Familiar (5 names)	8.26 (8.0)	7.26 (6.3)	11.14 (10.8)	7.68 (7.1)
Unfamiliar (5 names)	5.79 (7.8)	5.76 (5.2)	5.72 (3.9)	5.19 (6.5)
Mean	7.03 (7.8)	6.51 (5.8)	8.43 (8.4)	6.43 (6.9)

Values are mean (SD) in millimeters.
Names on List 1 (2) were the experimental stimuli for patients in Subgroup B1 (Subgroup B2). Scores on List 1 (2) of Subgroup B1 (Subgroup B2) were compared with scores for these names from patients not exposed to List 1 (2) (i.e., patients from Group A and those from Subgroup B2 or B1).

not exposed to the stimuli, divided by the SD for the patient's own experimental group. No significant correlations were found between the amount of memory priming on the one hand, and gender, age, preoperative anxiety (State-Trait Anxiety Inventory), duration of surgery, or type of mechanical ventilation, on the other (for all rs: $0.03 < |r| < 0.28$; Ps > 0.05). A higher correlation was found for preoperative anxiety as measured with the Hospital Anxiety and Depression Scale ($r = 0.38$, $P < 0.01$), which should be treated with caution, due to the number of statistical tests performed.

Discussion

No memory-priming effects were demonstrated, although all differences were in the predicted direction. Hence, the question as to whether memory priming in the Jelicic et al. (17) study was based on elaboration of new or unfamiliar associations (e.g., between first and last name) remains unanswered. The most parsimonious hypothesis, however, is that activation of existing memory representations (e.g., strengthening of either the first or the last name, or both separately) occurred in the Jelicic et al. (17) study.

The notion that familiarity of stimuli may be important for memory priming is in accordance with previous results in the category-production task in which patients are presented with examples of different word categories (targets) during GA, and postoperatively asked to generate examples of these categories. When easy, familiar words were used as targets, significant memory-priming effects were found (8,10), whereas the use of less familiar words resulted in no memory priming (24,25); too much elaboration may have been required for the targets presented in these latter studies. Statistically reliable advantages for high-frequent (familiar) words above low-frequent (less familiar) words, presented during GA, have been demonstrated recently (26).

Information processing in nonconscious states may differ in quality from that during consciousness. If this difference is established in future research, then there may be less reason to consider implicit memory for information during GA a sign of temporarily light or insufficient anesthesia.

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