Anesthesiology
73:52–61, 1990

Anesthesia with Abdominal Surgery Leads to Intense REM Sleep during the First Postoperative Week

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Characteristics of nocturnal sleep were investigated in six patients after anesthesia and cholecystectomy and in another six after anesthesia and gastroplasty. All night polysomnographic recordings were obtained while each patient slept in a private surgical ward room through two nights before and five or six nights after operation. Anesthesia included thiopental, N_2O, isoflurane, and fentanyl. Postoperative analgesia was provided with parenteral morphine. Other aspects of care were routine. Nocturnal sleep was markedly disturbed after both surgical procedures. Throughout the operative night and subsequent one or two nights, sleep was highly fragmented with the usual recurring cycles of sleep stages completely disrupted. Slow wave sleep was suppressed and rapid eye movement (REM) sleep virtually eliminated. During the following 2–4 nights, as other aspects of sleep recovered, REM sleep reappeared and then increased to greater than the preoperative amount. This increased REM sleep was marked by a heavy density of eye movement activity along with frequent patient reports of unusually distressing dreams or vivid nightmares. It is concluded that anesthesia with upper abdominal surgery leads to a severe disruption of nocturnal sleep followed by the release of highly intense REM sleep about the middle of the first postoperative week. (Key words: Anesthesia: complications. Surgery: complications. Sleep: REM.)

ALTHOUGH not commonly recognized, several of the most important cardiac, neurologic, and psychiatric complications of anesthesia and surgery appear most frequently about the middle of the first postoperative week, *i.e.*, between the second and fifth postoperative days. Acute myocardial infarction in the perioperative period peaks in incidence on the third to fifth day after surgery[1,2] as may episodes of myocardial ischemia in patients with coronary artery disease.[3,4] Patients with cerebral vascular disease are at an increased risk of stroke at this time.[5,6] Delirium of unknown cause, a common complication of anesthesia and surgery in the elderly, almost always appears in this period.[7,8] Observant nurses and physicians know that patients frequently experience nightmares and/or a slump in mood around the third or fourth postoperative day, and research has shown a measurable decline in several indices of psychomotor performance.[9]

Unlike the factors that precipitate most other complications of anesthesia and surgery, the specific triggers of each of these events remain mysterious. Why they should appear after a delay of 2 or more days from the time of operation when the major known neurohumoral "stresses" have subsided[10,11] is not understood. The reductions of arterial oxygen tension that develop in the first 2–3 days after thoracic and upper abdominal surgery[12] are usually too modest and procedure-specific to account for them. The lack of sound knowledge about the genesis of these complications is a critical problem because it precludes the development of reliable means of prevention. This somewhat neglected field of perioperative medicine deserves the interest and attention of anesthesiologists.[13]

A potential determinant of these delayed complications that has received scant attention to date is disturbed natural sleep. It is known that minor surgery to repair an inguinal hernia leads to a disruption of sleep through 4 postoperative nights, with reductions of both rapid eye movement sleep (REM sleep) and the slow wave portion of non-REM sleep (SWS) followed by their gradual recovery.[14] It is also known that major surgery followed by care in an ICU curtails overall sleep severely and nearly abolishes both REM sleep and SWS throughout the ICU period,[15] disturbances that are usually attributed to the ICU environment. How natural sleep is affected by major surgery without ICU care appears not to have been systematically investigated.

Our hypothesis was that anesthesia and major abdominal surgery followed by routine postoperative care would suppress or eliminate REM sleep for one or two nights and then bring about a rebound increase of REM sleep during subsequent nights. From the characteristics of REM sleep rebound observed in other settings,[16,17] we suspected that a rebound after surgery might be associated with a greater than normal eye movement activity, indicating an increase in REM sleep intensity. We further hypothesized that such a state of REM sleep, if it developed in the postoperative setting, might exaggerate some of the known physiologic concomitants of REM sleep, such as episodic disorders of breathing with hypoxemia[18] and sharp fluctuations in heart rate and blood pressure.[19] If these changes did appear about midweek after anesthesia and surgery, we wondered if they might play a role in the genesis of one or more of the delayed complications noted above.

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Received from the Department of Anesthesia, University Hospital and the University of Western Ontario, London, Ontario, Canada. Accepted for publication February 26, 1990. Supported by the Medical Research Council of Canada, Grant No. MA 6443.

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The purpose of this study was to begin to explore this series of hypotheses by determining the characteristics of nocturnal sleep through several nights of sleep after anesthesia and upper abdominal surgery.

Methods

The protocol for the study had been approved by the Health Sciences Standing Committee on Human Research of the University of Western Ontario.

The subjects were patients scheduled for elective upper abdominal surgery, either cholecystectomy or gastroplasty. Exclusion criteria included age over 45 yr; evidence of cardiovascular, respiratory, metabolic, or neurologic disease; a history to suggest a sleep disorder; and the regular use of any medication. Also eliminated were patients undergoing cholecystectomy who were more than 30% above ideal body weight. Each patient was fully informed of the nature of the study and gave written consent.

Sleep was monitored through the two nights immediately prior to surgery and the five or six consecutive nights thereafter. The first of the two nights before surgery was provided for adaptation to the recording environment; the second was taken as the preoperative control. Throughout all nights of the study, the patient slept in a standard private surgical floor room located next to a separate room containing the sleep recording equipment.

On the day of operation anesthesia was induced with thiopental and then maintained with isoflurane, nitrous oxide, fentanyl, and pancuronium. Cholecystectomy or gastroplasty was performed through an upper midline abdominal incision. Upon arousal from anesthesia, the patient was transferred to the recovery room and then to the surgical ward. Postoperative analgesia was provided through the first 2 or 3 postoperative days with morphine 0.15–0.20 mg/kg ideal body weight im every 4 h as needed and then with codeine 30 mg po every 4 h as needed. Nausea and/or vomiting were treated with diphenhydramine 50 mg. Otherwise, no sedative or hypnotic medication was administered, either before or after operation. All remaining aspects of perianesthetic and perioperative care were routine.

To characterize nocturnal sleep, we recorded the electroencephalogram (EEG) from scalp electrodes located at the A1–C4 and A2–C3 positions; the electrooculogram (EOG) from unipolar electrodes placed at the lateral canthus of each eye; and the electromyogram (EMG) from bipolar electrodes positioned in the submental area. The methods of attaching and arranging the electrodes were previously described.[20] All electrode wires were drawn together in a loose "ponytail" arrangement that permitted normal movement in bed and easy disconnection for washroom visits. Cables carrying the EEG, EMG, and EOG signals passed through a wall to the adjacent monitoring room where the signal recording equipment was located. All signals were inscribed on a polygraph recorder (Grass 78D) run at a paper speed of 10 mm/s.

On each night of the study, recordings began with "lights out" at about 2300 h and continued until the usual time at which patients are awakened by the nursing staff, about 0600 h. Throughout this period the patient's room was kept dark and completely free of noise and activity, apart from routine visits by the attending nursing staff. Upon awakening in the morning, those patients who had undergone cholecystectomy were asked about their recollection of dreams.

Sleep was staged for each 30-s interval of each night using standard EEG, EOG, and EMG criteria.[21,§] The number of rapid eye movements in REM sleep was counted from the characteristic deflections in the recorded EOG signals. The following variables of sleep were then determined: 1) the time in bed, 2) the total sleep time, 3) the number of awakenings during the sleep period, and 4) the percent of time spent in each sleep stage, *i.e.*, non-REM (NREM) Stage 1, 2, and SWS (slow wave sleep) and REM sleep. Certain specific characteristics of REM sleep were also determined: 1) the REM sleep latency, *i.e.*, the time from sleep onset to first appearance of REM sleep; 2) the REM density, *i.e.*, the number of eye movements per minute of REM sleep; and 3) the total REM activity, *i.e.*, the total number of eye movements throughout all periods of REM sleep in the night.

In addition to monitoring sleep, we noted changes or events that may have acted to disrupt sleep, such as pain, opioid administrations, fever, nighttime visits by nurses, use of a nasogastric tube, and the occurrence of anesthetic or surgical complications. The severity of pain was estimated each evening in patients who had undergone cholecystectomy by having the patient mark his or her perception of pain intensity on a standard 10 cm vertical visual analogue scale. The pain score was the measured distance from the bottom or "no pain" end of the scale. The total amount of morphine and/or codeine administered was determined for each patient during two periods of each study day: the nighttime period, *i.e.*, the interval from 4 h before sleep onset until 30 min before the final morning awakening, and the daytime period,

§ Rechtschaffen A, Kales A: A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Los Angeles, BIS/BRI, UCLA, 1977.

Sleep researchers have arbitrarily divided sleep into Stages 1, 2, SWS (slow wave sleep), and REM sleep. Stages 1, 2, and SWS make up NREM sleep. Stage 1 is a transient phase usually occurring at sleep onset. Stage 2 is the predominant sleep stage and consists of low amplitude brain waves together with sleep spindles and K complexes. Stage SWS is associated with high-voltage synchronized slow brain waves. Stage REM is characterized by rapid bilaterally synchronous eye movements and loss of skeletal muscle tone.

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TABLE 1. Subject Characteristics

	Cholecystectomy (n = 6)	Gastroplasty (n = 6)
Age (yr)	35 ± 8	33 ± 5
Sex	4 males/2 females	3 males/3 females
Height (cm)	174 ± 11	173 ± 6
Weight (kg)	83 ± 12	153 ± 11
Hemoglobin (g/l)	148 ± 9	142 ± 12
Vital capacity (l)	4.4 ± 0.8	4.2 ± 0.7
Blood pressure (mmHg)		
Systolic	115 ± 18	130 ± 14
Diastolic	73 ± 8	83 ± 8

Values are mean ± SD.

i.e., the remainder of the 24-h day. To facilitate comparisons, we converted each opioid administration to a morphine dose equivalent per kilogram of ideal body weight, assuming a morphine:codeine potency ratio of 10:1. The oral temperature was measured each night at 2200 h.

Because we could not assume that factors disrupting sleep would be the same after cholecystectomy and gastroplasty, the results after each procedure were considered separately. The values of measured variables were represented by the mean ± 1 SD. Potential differences between study nights were assessed by the analysis of variance (ANOVA) for repeated measures and the least significant test when indicated. A P value of less than 0.05 was considered significant.

In presenting the results, we describe the night immediately after surgery as the operative night and the succeeding nights as postoperative nights numbered 1 through 5. In this system postoperative night 2 is actually the third night after surgery.

Results

Six patients were studied after cholecystectomy (C) and six after gastroplasty (G). Their preoperative characteristics are listed in table 1. Five of the six patients who underwent cholecystectomy were studied through six nights after surgery; the sixth patient and all patients who underwent gastroplasty were studied through five postoperative nights. All anesthetic and surgical procedures proceeded without immediate complication.

The postoperative period was associated with several events that may have disturbed nocturnal sleep. All patients were awakened two to three times on each of the first 2–3 nights after surgery for opioid administration and/or nursing checks. All experienced pain for which they received morphine and then codeine in progressively decreasing morphine dose equivalents (table 2). A slight elevation in temperature occurred regularly on postoperative nights 1 and/or 2 (table 2). Patients who underwent gastroplasty had a nasogastric tube in place for the first 2 postoperative days, whereas those who underwent cholecystectomy did not.

Three patients presented evidence of minor respiratory complications on 1 or more days after surgery. A patient who underwent cholecystectomy developed an unproductive cough on the night immediately following operation. Another who had had a gastroplasty presented with a slightly productive cough on the first and second postoperative days together with radiologic evidence of a left lower lobe segmental collapse. Still another patient after gastroplasty was found to have subsegmental atelectasis on a chest x-ray taken on the second day after operation.

The characteristics of sleep were nearly the same on the adaptation and the preoperative control nights in both cholecystectomy and gastroplasty groups (table 3). The total sleep time on each of these nights was within the expected normal limits, although tending toward the lower portion of the normal range.[21] The percentage of REM sleep was also low normal in both groups on both nights, and the proportion of SWS tended toward the upper limit of normal values.[21]

TABLE 2. Details of Postoperative Course by Night

			Postoperative				
	Preoperative	Operative	1	2	3	4	5
Cholecystectomy							
Pain score (mm)	—	42 ± 18	36 ± 14	34 ± 20	28 ± 26	26 ± 21	14 ± 15
Morphine dose equivalent (mg/kg)							
Daytime	—	0.43 ± 0.14	0.57 ± 0.14	0.42 ± 0.13	0.24 ± 0.08	0.12 ± 0.10	0.09 ± 0.10
Nighttime	—	0.39 ± 0.08	0.33 ± 0.11	0.21 ± 0.11	0.10 ± 0.06	0.05 ± 0.07	0.04 ± 0.05
Temperature (° C)	36.8 ± 0.3	37.2 ± 0.8	37.7 ± 0.2*	37.5 ± 0.7*	36.7 ± 0.3	37.0 ± 0.3	36.4 ± 0.8
Gastroplasty							
Morphine dose equivalent (mg/kg)							
Daytime	—	0.21 ± 0.13	0.57 ± 0.14	0.52 ± 0.07	0.48 ± 0.11	0.26 ± 0.09	—
Nighttime	—	0.43 ± 0.12	0.41 ± 0.10	0.39 ± 0.13	0.28 ± 0.07	0.13 ± 0.09	—
Temperature (° C)	36.9 ± 0.4	36.6 ± 0.8	37.4 ± 0.3	37.9 ± 0.8*	37.3 ± 0.8	37.1 ± 0.5	—

Values are mean ± SD.

* Significantly greater than preoperative value.

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TABLE 3. Major Variables of Overall Sleep by Night

	Adaptation	Preoperative	Operative	Postoperative 1	Postoperative 2	Postoperative 3	Postoperative 4	Postoperative 5
Cholecystectomy								
Time in bed (min)	439 ± 39	394 ± 49	393 ± 71	409 ± 56	387 ± 48	414 ± 55	388 ± 51	402 ± 54
Total sleep time (min)	348 ± 57	327 ± 69	282 ± 34	318 ± 40	311 ± 34	329 ± 61	305 ± 119	353 ± 13
Awakenings (no.)	10 ± 5	9 ± 4	17 ± 8	21 ± 17	15 ± 12	12 ± 5	9 ± 8	7 ± 3
Sleep stage times (% total sleep time)								
NREM-1	7 ± 2	10 ± 5	16 ± 9	18 ± 12	15 ± 9	13 ± 10	14 ± 20	6 ± 1
NREM-2	52 ± 3	50 ± 8	80 ± 7*	70 ± 13*	50 ± 16	40 ± 13	34 ± 13†	37 ± 11
NREM-SWS	20 ± 7	23 ± 8	3 ± 4†	6 ± 8†	15 ± 12	20 ± 10	26 ± 14	27 ± 8
REM	20 ± 6	18 ± 6	0 ± 0†	6 ± 6†	20 ± 12	26 ± 12	25 ± 7	30 ± 8*
Gastroplasty								
Time in bed (min)	449 ± 39	399 ± 63	454 ± 34*	443 ± 29*	444 ± 35*	408 ± 40	419 ± 64	
Total sleep time (min)	376 ± 42	360 ± 64	334 ± 70	273 ± 107	334 ± 49	324 ± 49	343 ± 70	
Awakenings (no.)	7 ± 3	4 ± 3	17 ± 4*	22 ± 12*	12 ± 4*	7 ± 4	6 ± 3	
Sleep stage times (% total sleep time)								
NREM-1	5 ± 3	6 ± 5	15 ± 17	22 ± 28*	14 ± 11	10 ± 7	5 ± 4	
NREM-2	49 ± 8	49 ± 8	79 ± 16*	68 ± 25*	67 ± 14*	51 ± 10	38 ± 10	
NREM-SWS	25 ± 13	27 ± 14	6 ± 8†	8 ± 11†	12 ± 11†	20 ± 10	30 ± 11	
REM	19 ± 4	19 ± 5	0 ± 0†	1 ± 2†	5 ± 7†	18 ± 7	26 ± 6*	

Values are mean ± SD.
* Significantly greater than preoperative value.
† Significantly smaller than preoperative value.

On each night studied after operation the total sleep time was not detectably different from preoperative control (table 3). However, the structure of sleep was markedly altered. On the operative night sleep was interrupted frequently by spontaneous awakenings (table 3) such that the normal pattern of sleep stage cycles was completely disrupted (fig. 1). SWS time was reduced and REM sleep abolished while Stage 2 sleep was increased in a reciprocal way (table 3). Similar but less marked changes were usually apparent through an additional night after cholecystectomy (*i.e.*, postoperative night 1) and the next two nights following gastroplasty (*i.e.*, postoperative nights 1 and 2). During the remaining nights of study, the continuity of sleep, the cycles of sleep stages, and the amount of SWS all gradually returned toward their preoperative values or characteristics (table 3).

REM sleep behaved somewhat differently in the nights after surgery in that after being abolished in the first one or two nights, it reemerged and then increased to greater than preoperative control (table 3, fig. 1). The particular nights of REM sleep reemergence and then increase varied considerably. Among individual patients REM sleep reappeared on postoperative night 1 (C, n = 4; G, n = 1), night 2 (C, n = 2; G, n = 3), or night 3 (G, n = 2) and then increased on postoperative night 2 (C, n = 2), night 3 (C, n = 4; G, n = 2), night 4 (C, n = 4; G, n = 5), and/or night 5 (C, n = 4). The increments were due primarily to lengthening of individual REM sleep periods rather than a greater number of periods (fig. 1).

Due to the considerable individual variability in the night-by-night time course of REM sleep changes after operation, we examined the specific characteristics of REM sleep in these nights with respect to the first postoperative night in which REM sleep reemerged. We called this first night R_1 and the succeeding nights, R_2, R_3, and R_4 (table 4). We also considered the REM sleep characteristics of the night in which REM sleep time was the greatest, calling this particular night R_{PEAK} (table 4). The R_{PEAK} night of individuals was night R_2, R_3, or R_4, which corresponded to postoperative nights 2, 3, 4, or 5.

When analyzed in this manner, REM sleep time increased on R_3 and R_4 after cholecystectomy (table 4). The REM density, the eye movement frequency, became greater on R_3 after cholecystectomy and on R_2 after gastroplasty. The usual pattern of eye movements, *i.e.*, intermittent or phasic bursts, was maintained. The increased REM density, combined with the trends to greater REM sleep time, resulted in a substantial increment in the total REM activity, *i.e.*, the total number of eye movements in REM sleep on R_3 and R_4 after cholecystectomy and on R_2 after gastroplasty. The REM sleep time, the REM density, and the total REM activity were also greater on R_{PEAK} (table 4).

Because it had been established that REM sleep time is suppressed by morphine in a potent and linear dose-related fashion[22,23] and because opioid was administered during the nights of REM sleep after surgery, we further examined postoperative REM sleep characteristics by comparing the observed REM sleep times to those that would be predicted from the effect of the opioid per se. To make this comparison we plotted the REM sleep time of each night of each patient in relation to the amount of

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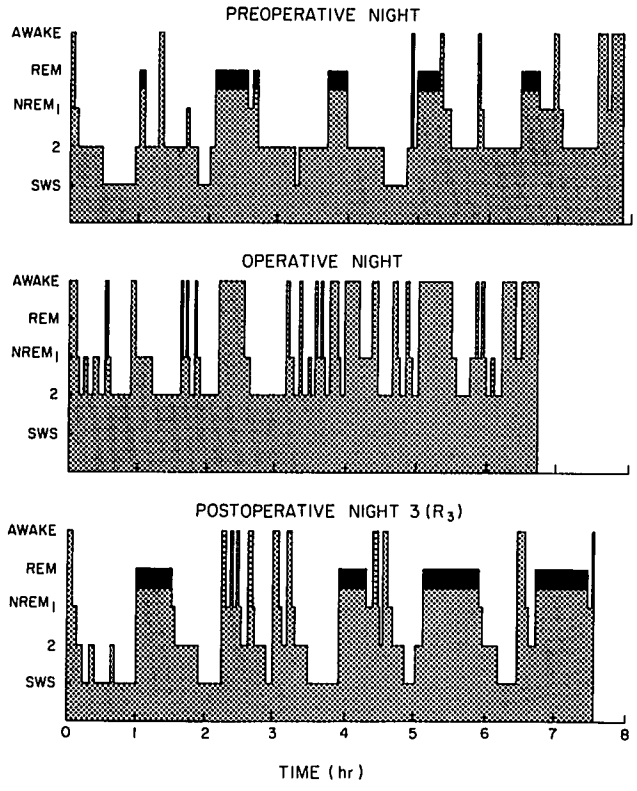

FIG. 1. Nocturnal sleep of a patient who underwent anesthesia and cholecystectomy. All night somnograms are shown for the preoperative control night (*top*), the operative night (*middle*), and postoperative night 3 (*bottom*). On the preoperative control night the pattern of sleep was normal. On the night of operation sleep was interrupted frequently by spontaneous awakenings, such that the normal cycles of sleep stages were completely disrupted. Neither REM sleep nor slow wave sleep was observed. On postoperative night 3 a semblance of normal sleep continuity and pattern of sleep cycles was evident again, but the total amount of REM sleep was greater than that on the preoperative control night.

opioid administered that night, expressed as a morphine dose equivalent. To these plots we added a predicted morphine dose:REM sleep effect curve (fig. 2). This curve was constructed between two end points that were observed in each subject, which were 1) on the y-axis, the percent REM sleep time in the night before surgery when no opioid was administered, and 2) on the x-axis, the morphine dose equivalent associated with complete suppression of REM sleep on the night of operation. (The dose of opioid that abolished REM sleep on the night of operation was just greater than that which allowed a small amount of REM sleep on a subsequent night.) The curve between these end points was made linear in keeping with previous observations.[22,23] When the REM sleep times observed after surgery were compared with those of the predicted morphine dose:effect curve, the observed times were found to be greater on nights R_2, R_3, R_4, and R_{PEAK} after cholecystectomy and on R_2, R_3, and R_{PEAK} after gastroplasty. These increments above predicted were termed "REM sleep excess" (table 4). The night-by-night trend of REM sleep excess paralleled that of added REM density after both cholecystectomy and gastroplasty, with both variables peaking in value on R_2 and R_3 after cholecystectomy and on R_2 after gastroplasty (fig. 3).

The patients who underwent cholecystectomy reported pleasant dreams on one or more of the study nights (table 5). In addition, five of the six patients experienced unusually distressing dreams or vivid nightmares on one or two of the postoperative nights of REM sleep recovery. The bad dreams or nightmares appeared to be most frequent on R_2 and R_{PEAK} (table 5).

In examining the results for potential correlates of the changes in sleep after surgery, we found that those nights in which sleep was most severely disrupted, *i.e.*, the nights of most frequent awakenings and marked suppression of SWS and REM sleep (table 3), were the nights in which both the opioid dose and the pain intensity were the greatest (table 2). In addition, the night-by-night pattern of recovery of REM sleep appeared to mirror the progressive reduction of nighttime morphine dose equivalents after both surgical procedures, with a relative delay in recovery after gastroplasty paralleling a delay in withdrawal of the opioid (fig. 4). The recovery of REM sleep after cholecystectomy (table 3, fig. 4) also corresponded to the gradual dissipation of pain (table 2). No other relationships to postoperative changes or events were observed.

Discussion

To our knowledge, this is the first study of sleep after anesthesia and abdominal surgery conducted in a typical postsurgical ward setting. Our hypothesis focused interest on the changes in REM sleep. On the first nights after surgery, REM sleep was nearly completely abolished. On subsequent nights it reemerged and then increased to greater than the preoperative amount. The increase of REM sleep was marked by a disproportionate increment in the number of rapid eye movements in REM sleep and frequent reports of distressing dreams or vivid nightmares. This previously unrecognized state of highly intense REM sleep about midweek after anesthesia and surgery is potentially important as a source of added physiologic disturbance and/or stress.

To assess sleep in a typical postsurgical setting, we had established a sleep monitoring facility adjacent to a private room on a general surgical ward. Prior to the study we had monitored overnight sleep in eight inexperienced nonpatient volunteers in this setting and found that their sleep was completely normal and consistent for three consecutive nights.[20] Accordingly, we considered this environment to be acceptable for a study of this nature.

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TABLE 4. Variables of REM Sleep by Night of REM Sleep Recovery

	Preoperative	Operative	Postoperative				
			R_1	R_2	R_3	R_4	R_{PEAK}
Cholecystectomy							
REM sleep time (% total sleep time)	18 ± 6	0 ± 0†	6 ± 5†	24 ± 8	27 ± 12*	26 ± 9*	34 ± 5*
REM latency (min)	121 ± 72	—	186 ± 150	68 ± 43	92 ± 69	87 ± 79	36 ± 25
REM density (no. per min)	5 ± 4	—	2 ± 1†	6 ± 3	7 ± 4*	6 ± 4	7 ± 4*
Total REM activity (no.)	397 ± 379	—	46 ± 58†	441 ± 265	513 ± 523*	546 ± 429*	825 ± 458*
REM sleep excess (% total sleep time)	0 ± 0	—	3 ± 3	13 ± 10*	14 ± 15*	10 ± 14*	19 ± 10*
Gastroplasty							
REM sleep time (% total sleep time)	19 ± 5	0 ± 0†	12 ± 10†	21 ± 7	20 ± 6	37	28 ± 5*
REM latency (min)	112 ± 50	—	149 ± 114	78 ± 62	95 ± 101	5	96 ± 99
REM density (no. per min)	5 ± 1	—	5 ± 2	7 ± 2*	6 ± 2	5	7 ± 2*
Total REM activity (no.)	339 ± 140	—	162 ± 117	572 ± 287*	382 ± 205	564	657 ± 167*
REM sleep excess (% total sleep time)	0 ± 0	—	8 ± 9	14 ± 9*	9 ± 4* (n = 3)	25 (n = 1)	18 ± 7*

Values are mean ± SD.
* Significantly greater than preoperative value (with total REM activity considered as per cent of control).
† Significantly smaller than preoperative value.

To minimize the numerous variables that might influence a study of postoperative sleep, we investigated two upper abdominal surgical procedures that are performed commonly and in a consistent fashion at this institution, cholecystectomy and gastroplasty. The patient subjects were selected to be relatively young and completely free of medical disorders, apart from obesity in the gastroplasty group. The anesthetic techniques and the postoperative analgesic therapy were standardized. We monitored sleep through the same hours of each study night, *i.e.*, from about 2300 h to the usual time of morning awakening on the wards, about 0600 h. Although it is unlikely that this nighttime period included all periods of sleep in each 24-h day after surgery, we believe that it contained the most consolidated and consistent sleep of each study day. [To have extended this study to a 24 h period of monitoring would have required an enormous investment of resources. As it was, the study yielded approximately 80,000 individual 30-s epochs of sleep for analysis.]

The total sleep time of each of the two nights studied before surgery, *i.e.*, the adaptation night and the preoperative control night (table 3), was normal but in the lower

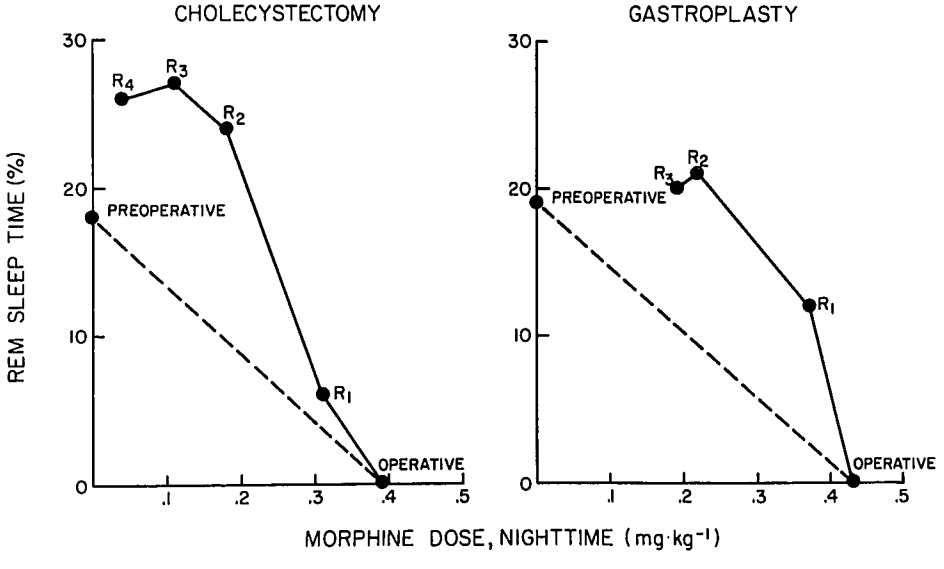

FIG. 2. REM sleep time in relation to the nighttime morphine dose equivalent of patients who underwent cholecystectomy (*left*) and gastroplasty (*right*). Data are plotted for the preoperative control night, the operative night, and postoperative nights R_1 to R_3 or R_4 (mean values only; see table 4 for SD). On the operative night when the nighttime morphine dose equivalent was the greatest, REM sleep was completely abolished. On the succeeding nights R_1 to R_3 or R_4, as the dose of opioid decreased, REM sleep reappeared and then increased in amount. The continuous line connects points of observed REM sleep times and nighttime morphine dose equivalents. The broken line depicts a predicted morphine dose:REM sleep effect curve. REM sleep time was greater than predicted on R_2, R_3, and R_4 after cholecystectomy and on R_2 and R_3 after gastroplasty. These increments above predicted are called "REM sleep excess."

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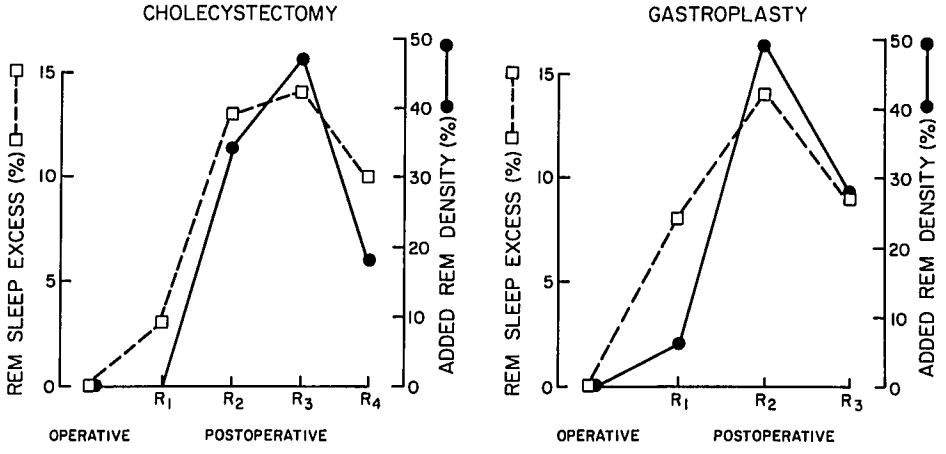

FIG. 3. Two characteristics of REM sleep after surgery, the REM sleep excess (*open squares, left ordinate*) and the added REM density (*closed circles, right ordinate*) of patients who underwent cholecystectomy (*left*) and gastroplasty (*right*). REM sleep excess, indicating the increase of REM sleep time over that expected from opioid effect, is shown as the percent of total sleep time (mean values; see table 4 for SD). Added REM density, indicating the increment in rapid eye movement frequency in REM sleep over preoperative control, is depicted as the percent increase (mean values). Data are displayed for the operative night and for postoperative nights R_1 to R_3 or R_4. Both an excess of REM sleep and a greater REM density appeared after surgery and both followed a similar night-by-night pattern of change.

portion of the normal range[21] and slightly less than what we had previously observed in our nonpatient volunteers in the same setting.[20] The percentage of REM sleep before surgery was also low normal and somewhat less than previously observed, and the percent SWS was high normal and slightly greater. These trends in sleep before operation are internally consistent with one another because a shorter sleep time is normally associated with both lesser REM sleep and greater SWS percentages.[21] This is because REM sleep is concentrated in the latter portion of sleep, whereas SWS appears primarily in the first one-third. Taken together, these trends suggest the presence of a factor that limited sleep before surgery and that was not operative in the previously studied volunteers. This factor was undoubtedly the early morning (0600 h) awakenings by the nursing staff. Because early morning awakenings are part of the normal routine of a surgical ward both before and after operation and because the associated trends in sleep were similar on both nights before operation, we accepted these preoperative sleep data as representative of sleep before operation and as an adequate baseline against which postoperative sleep data could be compared.

Anesthesia with cholecystectomy or gastroplasty markedly altered sleep through the five or six postoperative nights studied. The changes could be divided into two successive phases. First, there was a phase in which sleep was markedly disrupted, a phase that lasted two or three nights. Next, there was a phase during which sleep tended to recover toward control characteristics, and this was evident to the end of the study period. In the nights of the disruptive phase sleep was highly fragmented by frequent awakenings, SWS was severely reduced, and REM sleep was eliminated or nearly so (table 3, fig. 1). During the nights of the recovery phase the continuity of sleep and SWS gradually recovered while REM sleep reemerged and then increased to greater than the preoperative amount (table 3; figs. 1 and 4).

Our hypothesis directed particular interest to the characteristics of postoperative REM sleep. In an attempt to normalize data for the considerable variability in the time course of REM sleep changes, we examined this stage of sleep in successive nights beginning with the first night of its reappearance (calling these nights R_1, R_2, R_3, and R_4) and also in the individual night of greatest REM sleep time (R_{PEAK}). In addition to determining the standard characteristics of REM sleep, we estimated the amount of REM sleep that appeared to escape the potent depressive effects of opioid.[22,23] This variable, REM sleep excess, was the difference between the percent REM sleep time observed on each night after surgery and the time that would be normally expected in the presence of the concurrent nighttime dose of opioid (fig. 2). We believe that REM sleep excess reflects more closely the pressures for added REM sleep after surgery than does the REM sleep time per se because the latter was undoubtedly affected by the potent suppressive effects of opioid.[22,23]

The REM sleep time and/or the REM sleep excess increased on nights R_2, R_3, and/or R_4 after cholecystectomy and gastroplasty (table 4), these being postoperative nights 2, 3, 4, and/or 5. In addition, the REM density, the frequency of eye movements in REM sleep, became greater on nights R_2 or R_3 (table 4), indicating a dispro-

TABLE 5. Reports of Dreams

	Preoperative	Operative	Postoperative				
			R_1	R_2	R_3	R_4	R_{PEAK}
Pleasant dreams	3	1	2	0	2	2	1
Nightmares	0	0	1	4	1	1	3

Values are the number of subjects reporting; n = 6.

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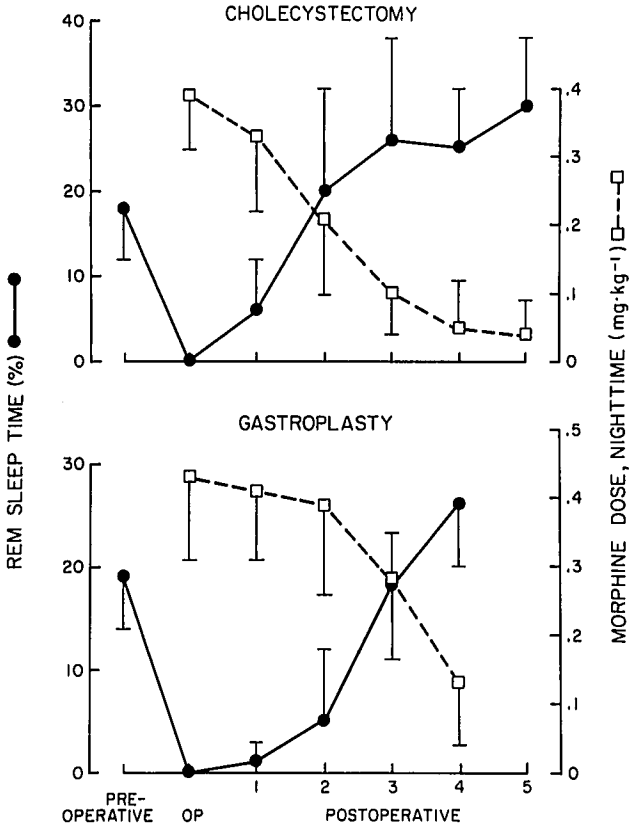

FIG. 4. REM sleep time (*closed circles, left ordinate*) together with nighttime morphine dose equivalents (*open squares, right ordinate*) in relation to each night of study for patients undergoing cholecystectomy (*top*) and gastroplasty (*bottom*) (mean ± SD). On the operative night after both procedures, REM sleep was completely abolished. On subsequent nights it reemerged and then increased to greater than preoperative control. The temporal pattern of REM sleep reemergence and increase after each surgical procedure appeared to mirror the progressive reduction of nighttime opioid dose.

portionate increment in eye movement activity. The night-by-night trends in REM sleep excess and added REM density after operation paralleled each other, and the peak increments of each appeared concurrently, suggesting a relationship between the two (fig. 3). On or about the night of greatest REM sleep excess and REM density, most patients who were questioned reported unusually distressing dreams or vivid nightmares (table 5).

The changes in REM density and dreaming about midweek after surgery imply a substantial difference in the nature of REM sleep at this time. Animal studies have shown that the intermittent rapid eye movements of REM sleep are linked to a constellation of other active neural phenomena in this state.[24] Accordingly, an increase in the eye movement activity can be taken to signify a generally more active or intense kind of REM sleep. Investigations of human subjects have found that vivid dreaming is normally associated with the REM portions of sleep[25] and that frightening dreams or nightmares tend to occur in the REM sleep periods with the greatest eye movement activity.[26] Thus, the finding of increased eye movement frequency together with nightmares on certain nights after surgery indicates that the REM sleep of these nights had increased intensity.

The magnitudes of the peak changes in REM sleep characteristics after operation were remarkable, especially after cholecystectomy. During the night of greatest REM sleep time, R_{PEAK}, corresponding to postoperative nights 2, 3, 4, or 5, the total REM activity was more than double control (table 4) and frightening dreams or nightmares were frequent (table 5). To our knowledge, such marked changes in total REM activity and dreaming have never been previously reported in a group of humans, even in the aftermath of pharmacologic suppression of REM sleep maintained for 2 weeks[16,17] or complete deprivation of REM sleep or all stages of sleep sustained for up to 6 days and nights.[27,28] On this basis we conclude that the REM sleep that appears about midweek after anesthesia and surgery is associated with an extraordinarily high level of intensity.

Several changes in sleep architecture observed in this study are qualitatively similar to those previously seen in the nights after inguinal hernia repair.[14] However, the initial fragmentation of sleep and reduction of REM sleep were comparatively less after hernia repair, and an increase of REM sleep time was not consistently observed. Thus, the effects of herniorrhaphy would appear to have been substantially less severe.

What are the determinants of the overall changes in sleep after surgery? Several factors, individually or combined, could have acted to cause the initial disruption of sleep, including anesthesia, fasting, environmental changes, postoperative hypoxemia, postoperative complications, an elevated body temperature, various elements of the endocrine/metabolic response to surgical trauma, opioid therapy, and/or pain. Although this study was not designed to examine the role of any of these factors directly, certain reasonable inferences can be made.

General anesthesia was unlikely to have played a major role in disrupting sleep after surgery because by itself it produces only a modest reduction of SWS for one night.[20] Furthermore, the changes in sleep after inguinal hernia repair are reported to be similar whether anesthesia is general or regional.[14] The reduction of caloric intake before and after surgery was also an unlikely determinant of sleep changes because even complete fasting reduces the amount of REM sleep only slightly, and it increases rather than decreases SWS.[29] It is doubtful that environmental factors, hypoxemia, or surgical complications played an important role because the patients of this study adapted well to their new sleep environment before operation, oxygen levels decreased as the disruptive phase

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ceased (unpublished observation), and the use of a nasogastric tube and the minor respiratory complications had no discernible independent effects on sleep. The postoperative elevation of body temperature (table 2), which might have disrupted sleep,[30] could not have contributed to the initial postoperative changes because the temperature increased only toward the end of the sleep disruptive period (table 2).

More likely to be underlying the initial disruption of sleep after operation were elements of the endocrine response to trauma and the presence of opioid and/or pain.

Increased amounts of corticosteroid can depress REM sleep,[31] and elevated brain catecholamines may do the same.[32] Thus, these elements of the endocrine response to surgical trauma could have contributed to the initial reduction of REM sleep after surgery. However, they do not explain the other sleep changes observed.

Morphine, when given in full analgesic doses to former opioid addicts or to healthy volunteers, increases awakenings from sleep, suppresses SWS, and often abolishes REM sleep.[22,23] The exceptionally powerful effects of this drug on sleep are remarkably similar to the pattern of changes that was seen in the first nights after cholecystectomy or gastroplasty (table 3; fig. 1). Furthermore, the nights of the greatest sleep disruption after each surgical procedure (table 3) corresponded to the nights during which full analgesic doses of opioid were given (table 2) and the nights of sleep recovery to the nights in which morphine was being withdrawn (table 2; fig. 4). Thus, both the nature and the time course of sleep disruption after operation can be almost completely accounted for by opioid.

Pain and/or noxious stimulation may have also played a role. The period of sleep disruption and the beginning of sleep recovery after cholecystectomy corresponded to the maximum pain intensity and the reduction of pain, respectively (table 2), although perhaps not as closely as they related to the pattern of nighttime morphine dose equivalents (table 2; fig. 4). The intensity of pain and the amount of opioid given are obviously interrelated, and their relative independent importance cannot be inferred. However, the remarkable similarity of the initial postoperative sleep changes to the effects of morphine alone and the apparent closer relationship of the period of sleep disruption to the time course of the nighttime morphine dose would lead us to favor the drug as the more proximate factor.

The determinants of the sleep recovery phase may be more complex. Disruptive factors, such as morphine and/or pain, persisted and gradually decreased during the nights of the recovery phase (table 2) and likely acted to check sleep recovery. The marked deprivations of REM sleep and SWS observed during the nights of the disruptive phase (table 3) would be expected to create a "pressure" for compensatory increases of each during the subsequent nights of recovery.[16,17,27,28,33] The added REM sleep time together with the greater total REM activity and the frequent nightmares observed during the nights of sleep recovery (tables 4 and 5) are all consistent with the kinds of changes often seen during nights of compensation for REM sleep deprivation. However, as previously indicated, the magnitudes of the peak changes in each of these REM sleep variables after operation were substantially greater than what would be expected on the basis of prior REM sleep deprivation alone,[16,17,27,28] suggesting that other factors may have also played a role. One additional factor may have been growth hormone. The blood level of growth hormone is reported to increase about the middle of the first postoperative week,[34] and added growth hormone is one of the few neurohumoral changes known to augment REM sleep time.[35]

From this analysis, we speculate that the principle causes of the sleep disruptive phase after surgery were opioid and/or pain. Elements of the endocrine response to trauma may have played a contributing role. The determinants of the subsequent sleep recovery phase were possibly the gradual withdrawal of the disruptive factors, the pressures for REM sleep compensation arising from prior deprivation, and perhaps increased growth hormone as well.

These postoperative changes in nocturnal sleep may be clinically important. The marked fragmentation of sleep may contribute to excessive daytime sleepiness after surgery, as it does in other circumstances,[36] and may thereby predispose to inactivity-related complications of the postoperative period. The highly intense REM sleep that appears about the middle of the first postoperative week may underlie the vivid nightmares often experienced by patients at this time because nightmares appear to be linked to the degree of REM sleep activity in other settings.[16,26] Although vivid nightmares might seem to be a trivial problem after major surgery, it is our impression that they are more frequent and more distressing to patients than, for example, postanesthetic nausea and vomiting.

More important is the possibility that the highly intense REM sleep that appears about midweek after operation is a source of physiologic stress that contributes to the genesis of certain delayed postoperative complications at this time, such as myocardial infarction, myocardial ischemia, and/or stroke in patients with coronary and/or cerebral vascular disease[1-6] and unexplained delirium in the elderly.[7,8] We suggest this possibility on the basis that normal REM sleep can produce striking changes in cardiovascular and respiratory function, including episodic swings in heart rate and blood pressure,[19] myocardial ischemia in patients with coronary artery disease,[37,38] and marked hypoxemia in the elderly or in those with chronic obstructive pulmonary disease.[18] More active or intense REM sleep would be expected to exaggerate at least some

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of these cardiorespiratory changes,[19,39] and perhaps more so in the context of the postoperative period when the baseline heart rate and blood pressure may already be elevated by noxious stimulation and arterial oxygenation is sometimes impaired.[12] If so, the highly intense REM sleep that develops after surgery could be a determinant of one or more of the delayed complications. This question deserves further research.[13]

The authors wish to thank the patients who participated in the study; the anesthesiologists, surgeons, and surgical nurses of University Hospital who cooperated with the standardization regimens; the administration of University Hospital who generously provided space on a surgical ward for a sleep monitoring facility; J. L. Clement and K. McNeill who helped establish and evaluate the facility; P. Y. K. Lok and A. J. Sharpe who developed the custom computer programs; and L. Nolan who assisted with the preparation of the manuscript.

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