

Dreaming and Electroencephalographic Changes during Anesthesia Maintained with Propofol or Desflurane

Kate Leslie, M.B., B.S., M.D., M.Epi., F.A.N.Z.C.A.,* Jamie Sleigh, M.B., Ch.B., M.D., Dip.App.Stat., F.A.N.Z.C.A.,† Michael J. Paech, M.B., B.S., D.R.C.O.G., F.R.C.A., F.A.N.Z.C.A., F.F.P.M.A.N.Z.C.A., F.R.A.N.Z.C.O.G.(Hon.), D.M.,‡ Logan Voss, B.Sc.(Hons.), Ph.D.,§ Chiew Woon Lim,|| Callum Sleigh, M.Sc.¶

Background: Dream recall is reportedly more common after propofol than after volatile anesthesia, but this may be due to delayed emergence or more amnesia after longer-acting volatiles. The electroencephalographic signs of dreaming during anesthesia and the differences between propofol and desflurane also are unknown. The authors therefore compared dream recall after propofol- or desflurane-maintained anesthesia and analyzed electroencephalographic patterns in dreamers and nondreamers and in propofol and desflurane patients for similarities to rapid eye movement and non-rapid eye movement sleep.

Methods: Three hundred patients presenting for noncardiac surgery were randomized to receive propofol- or desflurane-maintained anesthesia. The raw electroencephalogram was recorded from induction until patients were interviewed about dreaming when they became first oriented postoperatively. Using spectral and ordinal methods, the authors quantified the amount of sleep spindle-like activity and high-frequency power in the electroencephalogram.

Results: The incidence of dream recall was similar for propofol (27%) and desflurane (28%) patients. Times to interview were similar (median 20 [range 4–114] vs. 17 [7–86] min; $P = 0.1029$), but bispectral index values at interview were lower (85 [69–98] vs. 92 [40–98]; $P < 0.0001$) in propofol than in desflurane patients. During surgery, the raw electroencephalogram of propofol patients showed more and faster spindle activity than in desflurane patients ($P < 0.001$). The raw electroencephalogram of dreamers showed fewer spindles and more high-frequency power than in nondreamers in the 5 min before interview ($P < 0.05$).

Conclusions: Anesthetic-related dreaming seems to occur just before awakening and is associated with a rapid eye movement-like electroencephalographic pattern.

* Head of Anaesthesia Research, Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, and Honorary Associate Professor, Department of Pharmacology, University of Melbourne; † Professor of Anaesthesia, University of Auckland; ‡ Professor of Obstetric Anaesthesia, School of Medicine and Pharmacology, The University of Western Australia, Visiting Anaesthetist, Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, and Senior Anaesthetist, Department of Anaesthesia and Pain Medicine, King Edward Memorial Hospital for Women; § Research Fellow, University of Auckland; || Medical Student, Department of Anaesthesia and Pain Management, Royal Melbourne Hospital; ¶ Research Fellow, University of Auckland.

Received from the Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, Melbourne, Australia; Department of Pharmacology, University of Melbourne, Melbourne, Australia; Department of Anaesthesia, University of Auckland, Waikato, New Zealand; School of Medicine and Pharmacology, The University of Western Australia, Perth, Australia; Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, Australia; Department of Anaesthesia and Pain Medicine, King Edward Memorial Hospital for Women, Perth, Australia. Submitted for publication February 25, 2009. Accepted for publication April 23, 2009. Supported by a Project Grant (no. 08/005) from the Australian and New Zealand College of Anaesthetists, Melbourne, Victoria, Australia. ClinicalTrials.gov identifier NCT00446212; Australian Clinical Trials Registry number 012606000279527.

Address correspondence to Dr. Leslie: Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, Parkville, Victoria, 3050, Australia. kate.leslie@mh.org.au. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

PATIENTS frequently report that they have been dreaming during anesthesia. However, dreaming may actually occur as patients recover from anesthesia, when the brain is still affected by sedative concentrations of anesthetic drugs that are sufficient to activate endogenous sleep mechanisms and the patients enter a sleep state.^{1–3} If this hypothesis is correct, the raw electroencephalogram of patients who report dreaming may display characteristics of the raw electroencephalogram of natural sleep.

Dreaming occurs in both rapid eye movement (REM) and non-REM natural sleep. The electroencephalogram of non-REM sleep is characterized by loss of high-frequency electroencephalographic activity, the presence of sleep spindles (waxing and waning oscillations in the α [8–16 Hz] frequency range), K-complexes, and a varying amount of Δ (0.5–4 Hz) activity. In contrast, the electroencephalogram of REM sleep is very similar to the awake state (*i.e.*, broad-band high-frequency activity and lack of sleep spindles). REM sleep may be distinguished from the awake state by the presence of low muscle tone, rapid eye movements, and θ waves. The electroencephalographic signs of dreaming during natural sleep are not well described, but dream recall may be associated with more high-frequency activity⁴ and suppression of α power.^{5–8} However, the electroencephalographic patterns associated with anesthetic dreaming are unknown.

Patients receiving propofol for maintenance of general anesthesia often report higher incidences of dreaming than patients maintained with volatile anesthetics.^{9–12} One explanation is that propofol and volatile anesthetics have different pharmacological effects in the central nervous system.^{11,13,14} An alternative explanation is that propofol is associated with more rapid emergence from anesthesia than the older volatile anesthetics,¹⁵ allowing patients to report their dreams before they are forgotten. Luginbühl *et al.*¹⁶ compared patients receiving propofol and desflurane (a volatile agent with a more rapid recovery profile) and reported no difference in dream recall between the groups. However, the incidence of dreaming was low (3% overall) because patients were not interviewed until the first postoperative day.

To investigate these hypotheses further, we randomized patients to propofol or desflurane-maintained anesthesia and collected raw electroencephalogram from induction of anesthesia until completion of an early postoperative interview. Specifically, we tested the hypotheses that in patients presenting for noncardiac surgery under relaxant general anesthesia (1) propofol maintenance is associated with a higher incidence of dream recall

than desflurane maintenance, (2) the raw electroencephalogram distinguishes patients who report dreaming from those who do not, and (3) the raw electroencephalogram distinguishes patients receiving propofol and desflurane.

Materials and Methods

This randomized, double-blind controlled trial received prospective ethics committee approval at the Royal Melbourne Hospital, Melbourne, Australia; Royal Perth Hospital, Perth, Australia; King Edward Hospital for Women, Perth, Australia; and Waikato Hospital, Hamilton, New Zealand.

Eligible patients were aged 18–50 yr, were American Society of Anesthesiologists' physical status I–III, and were scheduled for elective noncardiac surgery under relaxant general anesthesia. Patients with inadequate English comprehension due to a language barrier, cognitive deficit, or intellectual disability, psychotic disorders, major affective disorders, or major drug abuse, or taking a benzodiazepine or more than two standard alcoholic drinks on the evening before surgery were excluded. Written informed consent was obtained from all recruited patients.

The primary endpoint was the incidence of dreaming reported on emergence from general anesthesia. Dreaming during anesthesia was defined as any experience that was described by the patient as dreaming and was thought by the patient to have occurred between induction of anesthesia and emergence after anesthesia. In our previous study, dreaming was reported on emergence in 36% of propofol patients and 20% of desflurane patients.¹ A sample size of 270 patients (135 patients per group) provides 80% power to detect this difference (36% *vs.* 20%; $\alpha = 0.05$). We therefore planned to recruit 300 patients in total. With 300 patients, the power to detect a 2-min difference between the two groups in the secondary endpoint of time to eye opening was 80% (14 min *vs.* 12 min; SD = 6 min; $n_1 = n_2 = 150$).

Patients were randomized from a computer-generated list** (block randomized by site), and randomization results were concealed until after consent was obtained. Patients were blind to group allocation. Intravenous access and routine monitoring were established. After skin preparation, a bispectral index (BIS) sensor (BIS-XP; Aspect Medical Systems Inc, Norwood, MA) was applied to the forehead of all patients, and electroencephalographic recording commenced. Anesthesia was induced with 1–2 $\mu\text{g}/\text{kg}$ fentanyl, propofol, and a muscle relaxant and was maintained with the randomized maintenance agent. In the propofol group, a target-controlled infusion device was used to target desired plasma propofol concentrations. In the desflurane group, desflurane admin-

istration commenced after induction with propofol. Anesthesia was titrated to BIS 40–55 during maintenance. Morphine, paracetamol, nonsteroidal antiinflammatory drugs, local anesthetic infiltration, peripheral nerve blocks, dexamethasone, and/or a 5-hydroxytryptamine₃ receptor blocker were allowed, but other opioids, nitrous oxide, midazolam, tramadol, ketamine, and major plexus and neuraxial blockade were prohibited. At the conclusion of surgery, after reversal of neuromuscular blockade and tracheal extubation, patients were taken to the postanesthesia care unit (PACU).

Patients were interviewed as soon as they became oriented to time, place, and person. We used the following standard questionnaire.¹⁷ What was the last thing you remember before going to sleep? What was the first thing you remember when you woke up? Can you recall anything between? Did you have any dreams during your anesthetic? Electroencephalographic recording continued until after the interview was complete. Interviewers were blind to group allocation and electroencephalographic data. If dreaming was reported, a narrative report was collected. All patients who reported dreaming were considered to be dreamers for the purpose of the analyses, whether or not they could remember the narrative of the dream.

Data Collection

Baseline data included demographic and surgical details, home dreaming recall frequency (0 = never; 1 = less than once a week; 2 = several times a week; 3 = almost every morning) and risk factors for awareness, including a past history of awareness, heavy alcohol or sedative drug use and anticipated difficult intubation. Clinical signs of inadequate anesthesia, including movement and autonomic signs (tachycardia, hypertension, sweating, and lacrimation) were recorded. Anesthesia duration was defined as the time from induction of anesthesia to the completion of wound closure. Times to eye opening, to orientation to time, place, and person, and to eligibility for PACU discharge (Aldrete score ≥ 9 ¹⁸) commenced at time of completion of wound closure.

Raw electroencephalographic data were collected in real time, and BIS data were downloaded from the monitor at the end of each case, both with specific patient consent and using research software provided by Aspect Medical Systems (once-per-minute recordings; smoothing = 15 s for BIS data; recordings with signal quality below 50 were removed from the analysis).

Electroencephalographic Analysis

The raw electroencephalographic signal was digitized at 128/s and 14-bit resolution. The signal was then bandpass filtered between 1 and 41 Hz by using a ninth order Butterworth filter. Segments with a maximum amplitude greater than 200 μV were rejected as artifacts. We hypothesized that recalled dreams would occur close to the time

** Available at www.randomization.com; accessed July 7, 2006.

of awakening; therefore, we concentrated the analysis on this period. Specifically, we analyzed 30-s segments of the electroencephalogram at the following time points: (1) the middle of the operation, (2) completion of wound closure, (3) eye opening, and (4) a sequence of times (-1 min, -2 min, -3 min . . . up to -20 min) before the dream interview.

The electroencephalographic waveforms were characterized in two different ways: spectral and ordinal. The power spectral density of the electroencephalographic segment was estimated by using the absolute value of the complex number that is output from the 'psd.m' Matlab function (Matlab 7.7.0; The Mathworks Inc, Natick, MA). We used this function because it is the standard nonparametric method, and it makes no assumptions about system linearity or noise inputs. It applies the Welch method to obtain averaged periodograms (by using a tapered Hamming window of length 64, 50% overlap, and 1-Hz frequency resolution). We attempted to develop a succinct description of the electroencephalographic power spectrum by using only a few parameters. To do this, it is necessary to separate the narrow-band oscillations in the electroencephalographic signal from the underlying broadband irregular activity. After taking the natural logarithm of the spectral density, this background activity was quantified by fitting a linear regression to the subset of frequencies in which there were no prominent oscillatory peaks. In our case, we used the frequencies that avoided the Δ (1–4 Hz) and α (8–16 Hz) oscillations – namely the 5–7 Hz and 17–35 Hz ranges. The strength of narrow-band oscillations was quantified by finding the peaks in the α and Δ wavebands (fig. 1). θ oscillations did not interfere with this process. Thus, the electroencephalographic spectrum could be described

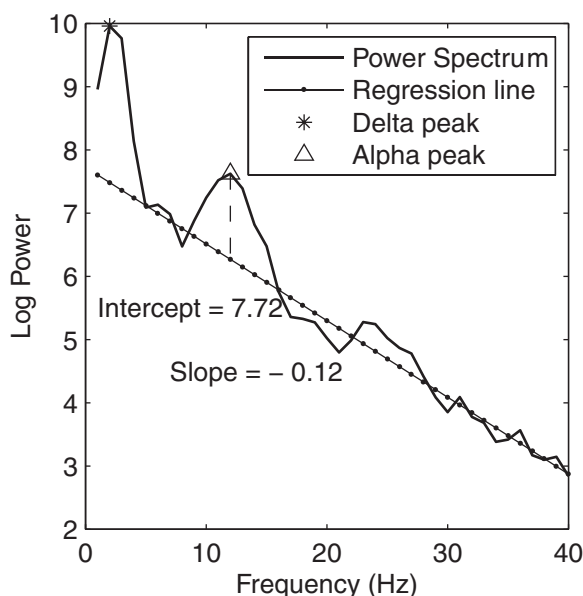


Fig. 1. Illustration of the method of obtaining parameters from the electroencephalographic power spectrum. The power spectrum is calculated as described in the text. The regression line describes the underlying broad band activity, and it is fitted to the power at frequencies (5–7 and 17–35 Hz).

by seven parameters: the broadband activity by the regression line slope and intercept, and the narrow-band oscillations by the height and frequency of the α and Δ peaks, and the spindle amplitude (the distance between the α peak and regression line underneath [the length of the vertical dotted line in fig. 1]). The power spectrum of natural non-REM sleep would be expected to show strong narrow-band oscillations in the α or Δ bands and a steep slope for the regression fit to the background activity. Conversely, the power spectrum of REM sleep would be expected to show no α or Δ oscillations and a flat gradient for the background activity.

A major problem with the use of Fourier methods of analysis for nonsinusoidal signals like the electroencephalogram is the presence of harmonics. For example, the spectral power at 16 Hz could reflect a pure 16 Hz sine-wave oscillation; alternatively, it could be generated by the second harmonic of a more angularly shaped 8-Hz oscillation. Bispectral analysis is suitable for detection and quantification of higher harmonics and is used in the BIS algorithm for this purpose. Another solution is to use an ordinal analysis that simply detects a sequence of peaks and troughs at the prescribed wavelength/"frequency" in the electroencephalographic signal. This method makes no assumptions about the shape or size of the peaks and troughs (as long as they are greater than a preset minimum threshold amplitude). This method is useful in the detection of oscillatory spindle-like activity in the electroencephalogram. The output from this method is the percentage of sampled data points that could be associated with a short ($\wedge\wedge$, 2peak-2trough) electroencephalographic pattern at the specific frequencies (10.68 Hz, 12.82 Hz, 16.02 Hz, and 21.36 Hz). We therefore used the ordinal method of analysis to complement (and check) the power spectral methods. During the course of the analysis, we tried various combinations of different settings for the spindle method (longer spindle sequences [up to 11 peaks and troughs] and different noise thresholds), but we found no improvement in discriminatory power.

Statistical Analyses

Continuous variables were graphed to assess their distribution. Normally distributed variables were described by using mean and SD and compared using two-tailed Student *t* tests. Skewed variables were described by using median and range and compared by using Wilcoxon rank sum test. Categorical variables were described by using number (%) and compared by using chi-square or Fisher exact test. Survival data (time to an event) were assessed by using log-rank tests. To minimize the biasing effect of a few outliers, the electroencephalographic parameters are presented as median (interquartile range). Predictors of dreaming from univariate analyses with *P* values less than 0.2 were all included in multivariate logistic regression models. Backwards elimination was used to eliminate nonsignificant predictors and to create parsimonious models. Inter-

Table 1. Baseline Characteristics of Patients Randomized to Propofol or Desflurane

Characteristic	Desflurane (n = 150)	Propofol (n = 150)
Age, yrs	36 ± 9	36 ± 9
Sex, female	102 (68)	102 (68)
ASA physical status		
I	69 (46)	74 (49)
II	75 (50)	67 (45)
III	6 (4)	9 (6)
Home dream recall		
< 1 per week	59 (39)	52 (34)
> 1 per week	62 (41)	72 (48)
Almost every day	29 (20)	26 (18)
At risk of awareness*	16 (11)	12 (8)
Operation type		
Gynecology	35 (23)	35 (23)
General	65 (44)	67 (45)
Other	50 (33)	48 (32)

Results are presented as mean ± standard deviation or number (percent).

* History of awareness, predicted difficult intubation, heavy alcohol intake or chronic opioid use. Some patients had more than one risk factor.

ASA = American Society of Anesthesiologists.

actions were tested (none significant – not shown). Results of these analyses are presented as adjusted odds ratios (OR) and 95% confidence intervals (CI). Statistical analyses were performed using Stata 8.2 (Stata Corporation, College Station, TX) and Matlab 7.7.0. $P < 0.05$ was accepted as statistically significant.

Results

A total of 330 patients consented to participation, and 300 were randomized. Thirty consenting patients were not randomized because their surgery was cancelled or rescheduled or because the anesthetic plan changed. Patients were similar at baseline (table 1). There was unequal gender distribution between the sites (100% female at King Edward Memorial Hospital for Women, 95% female at

Waikato, 58% female at Royal Melbourne Hospital, and 58% female at Royal Perth Hospital), but there were no statistically significant differences in the incidence of dreaming (38%, 24%, 23%, and 38%, respectively; $P = 0.07$). Patients randomized to propofol maintenance received higher total fentanyl doses and were more likely to move during anesthesia than patients randomized to desflurane (table 2). The range of BIS values during anesthesia was greater in propofol patients, and propofol patients had lower BIS values at eye opening and at the postoperative interview (table 3). Loss of BIS data because of signal quality less than 50 was not different between the propofol and desflurane groups during maintenance (1% [interquartile range 0–3%] vs. 0% [0–4%]; $P = 0.47$) or recovery (0% [0–13%] vs. 0% [0–7%]; $P = 0.20$).

Dreaming Results: Propofol versus Desflurane

Dreaming was reported on emergence by 27% of propofol patients and 28% of desflurane patients. Patients reported simple dreams about family, friends, work, and recreation. No patients reported awareness during anesthesia, and there were no dreams that were suggestive of intraoperative memory formation. Dreaming patients had higher home dream recall (table 4) and higher BIS values at interview (table 5). Thirty-five percent of gynecological surgery patients compared with 20% of other surgery patients recalled dreaming ($P = 0.08$). The only significant multivariate predictors of dreaming were dream recall greater than 1 per week (OR 3.01; 95% CI 1.53–5.93; $P = 0.001$), anesthesia duration of no more than 100 min (OR 1.96; 95% CI 1.07–3.60; $P = 0.03$), and BIS greater than 90 at interview (OR 1.89; 95% CI 1.05–3.45; $P = 0.035$).

Electroencephalographic Results: Dreamers versus Nondreamers

Suitable raw electroencephalographic data were obtained from only 150 patients due to difficulty in down-

Table 2. Intraoperative and Postoperative Characteristics of Patients Randomized to Propofol or Desflurane

Characteristic	Desflurane (n = 150)	Propofol (n = 150)	P Value
Fentanyl dose, μ g	100 (50–700)	150 (50–700)	0.03
Morphine dose, mg (n = 117)	10 (3–40)	10 (3–30)	0.82
Propofol target, μ g/ml	—	4.5 (2.5–8.0)	—
Desflurane concentration, %	5.8 (3.1–9.0)	—	—
Signs suggestive of awareness*	15 (10)	46 (31)	< 0.0001
Autonomic signs	8 (5)	12 (8)	0.36
Movement	9 (45)	37 (68)	< 0.0001
Duration of anesthesia, min	94 (27–320)	97 (25–467)	0.97
Time from wound closure to eyes open, min	9 (1–80)	10 (0–52)	0.47
Time from wound closure to orientation, min	17 (7–86)	20 (4–114)	0.10
Time from wound closure to PACU discharge, min	73 (12–213)	69 (10–157)	0.16
Time from eyes open to orientation, min	8 (0–57)	10 (0–100)	0.04
Dream reported	43 (29)	40 (27)	0.70
Narrative reported by patients reporting a dream	39 (91)	35 (88)	0.69

Results are presented as median (range) or number (percent).

* Autonomics signs = tachycardia, hypertension, lacrimation and sweating. Some patients had more than one risk factor.

PACU = postanesthesia care unit.

Table 3. Bispectral Index (BIS) Values in Patients Randomized to Propofol and Desflurane

Characteristic	Desflurane (n = 150)	Propofol (n = 150)	P Value
Median maintenance BIS	40 ± 6	38 ± 6	0.12
Minimum maintenance BIS	27 ± 8	25 ± 5	0.02
Maximum maintenance BIS	55 ± 11	58 ± 10	0.01
Range of maintenance BIS values	26 (8–79)	32 (11–68)	0.0004
BIS > 60 during maintenance, %	0 (0–47)	0 (0–25)	0.018
BIS 40–60 during maintenance, %	62 (0–100)	51 (0–100)	0.118
BIS < 40 during maintenance, %	37 (0–100)	45 (0–100)	0.15
BIS at wound closure	44 (25–96)	46 (22–86)	0.22
BIS at eye opening	80 (29–98)	75 (34–97)	0.0007
BIS at interview	92 (40–98)	85 (69–98)	< 0.0001

Median, minimum and maximum BIS values, and the difference between the minimum and maximum BIS value (i.e. range) were calculated for each patient, and then summarized within the desflurane and propofol groups. Results are presented as mean ± standard deviation or median (range).

loading raw electroencephalographic data and in achieving adequate signal quality in the other patients. Patients without raw electroencephalographic data were similar to patients with raw electroencephalographic data: mean age was 35 ± 9 versus 37 ± 9 yr ($P = 0.047$), 68% of patients were female in both groups ($P = 0.937$), American Society of Anesthesiologists status was 2–3 in 46% and 68% of patients ($P = 0.037$), and dream recall was 32% versus 23% ($P = 0.062$).

We undertook extensive analysis to characterize the raw electroencephalographic waveforms so that any putative parameter found to discriminate between the groups (dreamers *vs.* nondreamers and propofol *vs.* desflurane) could be linked to the underlying neurobiology of anesthesia, sleep, and dreaming. We have not reported most of this work because the best discriminatory parameters were simple: the spectral power in the high frequencies (greater than 20 Hz) and the relative amount of spindle activity. These two parameters are easily linked to REM and non-REM electroencephalographic patterns.

The differences in electroencephalographic parameters between the patients who reported dreams ($n = 34$) and those who did not ($n = 116$) were small. During surgery, there were no significant differences between dreamers and nondreamers, except that at wound closure the electroencephalographic slope parameter was less for dreamers than for nondreamers; and the log spectral power at 30 Hz was 4.8 (4.2 to 5.1) μV for dreamers versus 4.4 (3.8 to 4.9) μV for nondreamers ($P = 0.09$) (table 6).

A graphical demonstration of the mean changes in spectral power during the 20 min preceding the interview is shown in figure 2. Dreamers and nondreamers are represented by the colored and black mesh surfaces respectively. An 10-Hz spindle peak was lost as the patients approached the interview time, but the loss was more

Table 4. Characteristics of Nondreamers and Dreamers

Characteristic	Nondreamers (n = 217)	Dreamers (n = 83)	P Value
Age, yrs	36 ± 9	35 ± 8	0.55
Sex, female	147 (68)	57 (69)	0.88
ASA physical status			
I	102 (47)	41 (49)	—
II	102 (47)	40 (48)	—
III	13 (6)	2 (2)	0.44
Home dream recall			
< 1 per week	96 (44)	15 (18)	—
> 1 per week	85 (39)	49 (59)	—
Almost every day	36 (17)	19 (23)	< 0.0001
At risk of awareness*	22 (10)	6 (7)	0.44
Operation type			
Gynecology	45 (20)	25 (30)	—
General	99 (46)	33 (40)	—
Other	73 (34)	25 (30)	0.23
Propofol group	110 (51)	40 (48)	0.70
Fentanyl dose, μg	100 (50–700)	137 (50–550)	0.55
Morphine dose, mg	10 (3–40)	10 (2–30)	1.0
Propofol target, $\mu\text{g/ml}$	4.5 (2.5–8.0)	4.5 (2.5–7.0)	0.40
Desflurane concentration, %	5.8 (3.9–9.0)	5.8 (3.1–7.0)	0.10
Signs suggestive of awareness†	43 (20)	18 (22)	0.72
Autonomic responses	13 (6)	7 (8)	0.45
Movement	33 (15)	13 (16)	0.92
Duration of anesthesia, min	100 (25–467)	88 (28–320)	0.18
Time from wound closure to eyes open, min	10 (0–49)	9 (2–80)	0.66
Time from wound closure to orientation, min	19 (4–114)	18 (6–86)	0.50
Time from wound closure to PACU discharge, min	73 (10–213)	66 (12–185)	0.09
Time from eyes open to orientation, min	9 (0–100)	8 (1–40)	0.54

Results are presented as mean ± standard deviation, median (range), or number (percent).

* History of awareness, predicted difficult intubation, heavy alcohol intake, or chronic opioid use. Some patients had more than one risk factor. † Autonomic signs = tachycardia, hypertension, lacrimation, and sweating. Some patients had more than one risk factor.

ASA = American Society of Anesthesiologists. PACU = postanesthesia care unit.

pronounced in the dreamers than in the nondreamers (*i.e.*, the black mesh surface lies on top of the colored surface in this part of the figure). Conversely, high-frequency power was greater in the dreamers than the nondreamers close to the interview time.

More significant differences were observed just before the interview, when the electroencephalograms of dreamers showed more high-frequency (30 Hz) spectral power and fewer low-frequency (10.68 Hz) spindles (a REM-like pattern) than the nondreamers (fig. 3). There were no differences with respect to faster spindle oscillations.

Electroencephalographic Results: Propofol versus Desflurane

Propofol resulted in a more marked oscillatory peak in the frequency band 8–16 Hz (which corresponds to sleep spindle-like patterns) than desflurane (fig. 4), a more gentle

Table 5. Bispectral Index (BIS) Values in Nondreamers and Dreamers

Characteristic	Nondreamers (n = 217)	Dreamers (n = 83)	P Value
Median maintenance BIS	39 ± 6	38 ± 6	0.34
Minimum maintenance BIS	26 ± 7	25 ± 6	0.33
Maximum maintenance BIS	57 ± 10	55 ± 10	0.37
Range of maintenance BIS values	30 (3–79)	28 (10–68)	0.85
BIS > 60 during maintenance, %	0 (0–47)	0 (0–10)	0.73
BIS 40–60 during maintenance, %	42 (0–100)	42 (0–100)	0.62
BIS < 40 during maintenance, %	56 (0–100)	46 (0–100)	0.62
BIS at wound closure	44 (22–86)	46 (23–96)	0.93
BIS at eye opening	77 (29–98)	77 (35–97)	0.72
BIS at interview	88 (40–98)	91 (69–98)	0.002

Median, minimum and maximum BIS values, and the difference between the minimum and maximum BIS value (i.e. range) were calculated for each patient, and then summarized within the non-dreamer and dreamer groups. Results are presented as mean ± standard deviation or median (range).

underlying slope, a lower intercept, and larger and faster spindle frequency oscillations than the desflurane electroencephalogram (table 7). Desflurane patients had fewer spindle oscillations and more Δ power. There were no differences in the high-frequency components of the electroencephalogram. At eye opening, there were no significant differences between the groups, except that the peak frequency from the spectral analysis was 12 Hz for propofol patients and 9 Hz for desflurane patients ($P < 0.0001$) and the spindle amplitude for propofol was greater than for desflurane (1.49 [0.78 to 1.69] *vs.* 0.96 [0.69 to 1.66] log μ V; $P = 0.0002$). The ordinal analysis of electroencephalographic segments from the middle of surgery provided similar results, showing that propofol was associated with increased spindle activity, particularly in the 10–12 Hz range (table 7).

Table 6. Raw Electroencephalographic Parameters in Dreamers and Nondreamers

Parameter	Nondreamers (n = 75)	Dreamers (n = 75)	P Value
Wound closure			
Slope	−0.18 (−0.15 to −0.20)	−0.20 (−0.18 to 0.22)	0.03
Intercept	10.27 (9.78 to 10.68)	10.18 (9.79 to 10.53)	0.37
α Peak	9.79 (9.07 to 10.21)	9.64 (9.08 to 10.34)	0.75
Spindle amplitude	1.32 (0.91 to 1.71)	1.29 (0.99 to 1.78)	0.55
Δ Peak	10.47 (9.87 to 11.05)	10.72 (9.85 to 11.27)	0.43
Log spectral power at 30 Hz	4.4 (3.8 to 4.9)	4.8 (4.2 to 5.1)	0.09
Mid-surgery			
10.68 Hz spindle	10.52 (7.33 to 13.46)	10.75 (8.33 to 12.44)	0.18
12.82 Hz spindle	6.22 (4.58 to 8.75)	7.20 (5.57 to 8.96)	0.15
16.02 Hz spindle	3.12 (2.30 to 4.26)	3.44 (2.71 to 4.89)	0.27
21.36 Hz spindle	1.64 (1.15 to 2.50)	1.86 (1.46 to 2.51)	0.72
Peak frequency of spindle	10 Hz	11 Hz	0.36
Peak frequency of Δ	2 Hz	2 Hz	0.87

Results are presented as median (interquartile range). The spindle units are the percentage of electroencephalographic data points that could be associated with a spindle sequence. The units of spectral power are the natural logarithm with respect to 1 mV.

Discussion

This study found (1) no difference in dream recall between the propofol and desflurane groups, (2) more signs of cortical activation (more high-frequency power, fewer spindles, and higher BIS values) during recovery in patients reporting dreaming than not reporting dreaming, and (3) more spindle-like waves during maintenance of anesthesia with propofol than with desflurane.

Our finding of similar incidences of dream recall in patients randomized to propofol or desflurane is consistent with our hypothesis that the patients in the enflurane or isoflurane arm of previous randomized trials may have emerged more slowly from anesthesia and consequently had difficulty remembering any dreams.^{9–12} Lug-inbühl *et al.*¹⁶ reported similar recovery times and similar incidences of dreaming in the propofol and desflurane arms of their study, which is consistent with our result. However, their overall incidence of dreaming was low because they did not interview patients immediately upon emergence from anesthesia.¹ Our finding contrasts with our previous cohort study in which the incidence of dreaming was significantly higher in propofol patients than desflurane patients (36% *vs.* 20%).¹ This difference may be attributable to selection bias in the previous study.

The apparent electroencephalographic activation in dreamers could be caused by awakening (responsiveness to external stimuli), REM-like dreaming (internal cognitive activity that is disconnected from external stimuli and associated with reduced responsiveness), or artifact from frontalis electromyographic activity. These three states are difficult to separate on the basis of electroencephalographic analysis because of the fluctuating levels of alertness and stimulation during emergence from anesthesia. However, sustained awakening or increased electromyographic activity are unlikely to be the cause of the activated electroencephalogram in our patients who reported dreaming; both dreamers and nondream-

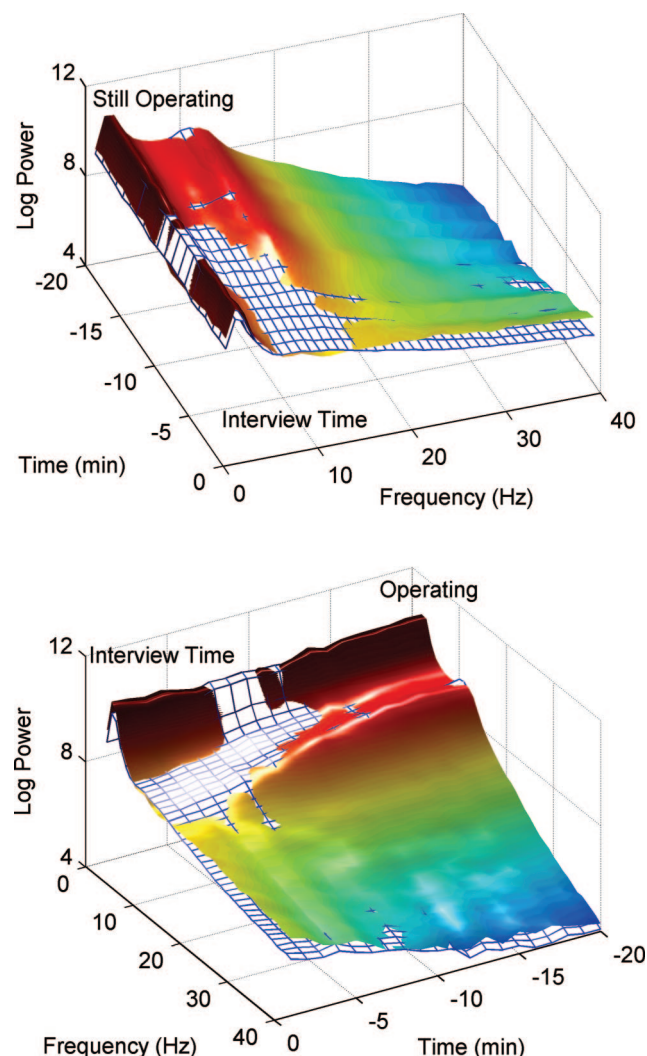


Fig. 2. Mean electroencephalographic power spectra of dreamers (colored surfaces) and nondreamers (blue mesh surfaces) in the 20 min before the interview. Both plots are of the same data, but they are rotated differently for ease of visualization. In the figures, the upper surface (which may be either blue mesh or rainbow color surface) hides the lower surface at each point in time and frequency.

ers were interviewed as soon as they were oriented, and there was no significant difference in the time from eye opening to interview between the two groups (table 4 and fig. 3). We therefore conclude that the increased high-frequency power and decreased sleep spindle in patients reporting dreaming was due to a REM-like state.

This conclusion is further corroborated by the similarity between our electroencephalographic findings and those of researchers who wake up patients from natural sleep.^{5,6,8} In these studies, suppression of electroencephalographic power in the α band was correlated with dream recall. During sleep states, α frequency oscillations consist mainly of sleep spindles, which are a definitive sign of stage 2 non-REM sleep. These spindles are generated in both natural sleep and general anesthesia,

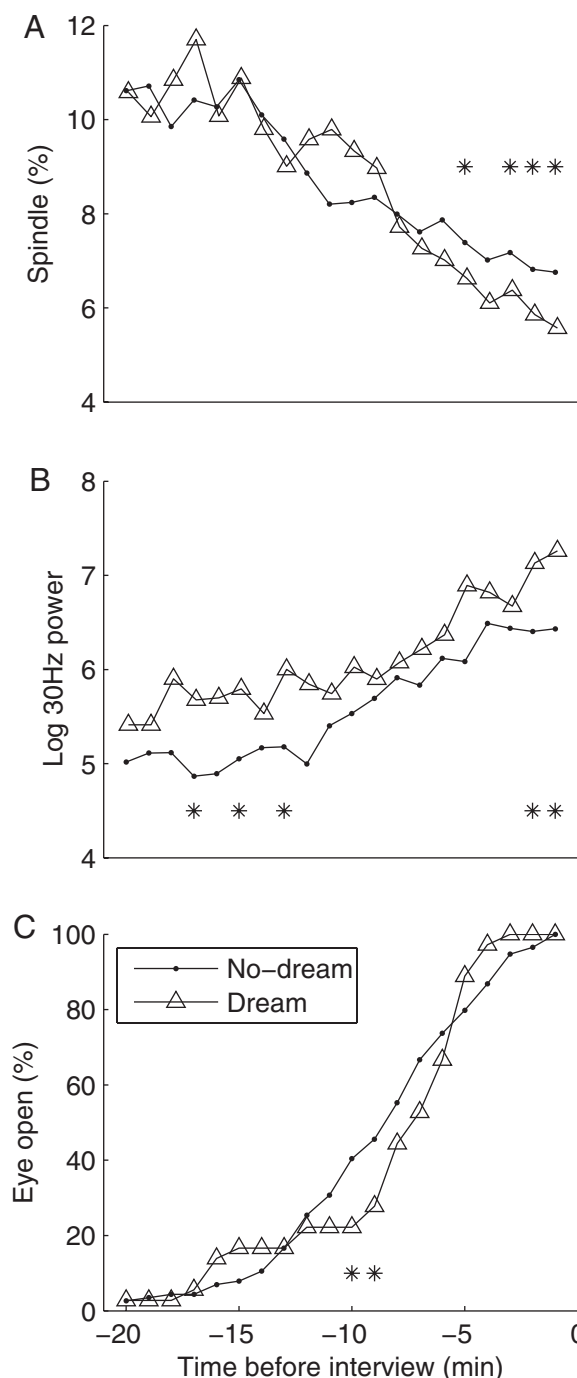


Fig. 3. Changes in percentage spindles, high-frequency power, and eye opening in the 20 min before interview in dreamers and nondreamers. (A) Changes in 10.68-Hz spindles. P values were as follows: $P = 0.01$ (–1 min), $P = 0.0009$ (–2 min), $P = 0.005$ (–3 min), $P = 0.09$ (–4 min) and $P = 0.04$ (–5 min). (B) Log 30-Hz power. P values were as follows: $P = 0.01$ (–1 min), $P = 0.02$ (–2 min), $P = 0.03$ (–13 min), $P = 0.04$ (–15 min) and $P = 0.03$ (–17 min). (C) Percentage of patients who had opened their eyes at each time point. P values were as follows: $P = 0.02$ (–9 min), $P = 0.03$ (–10 min). Results are presented as mean (SEM). * Significant difference ($P < 0.05$) between the groups at that time point.

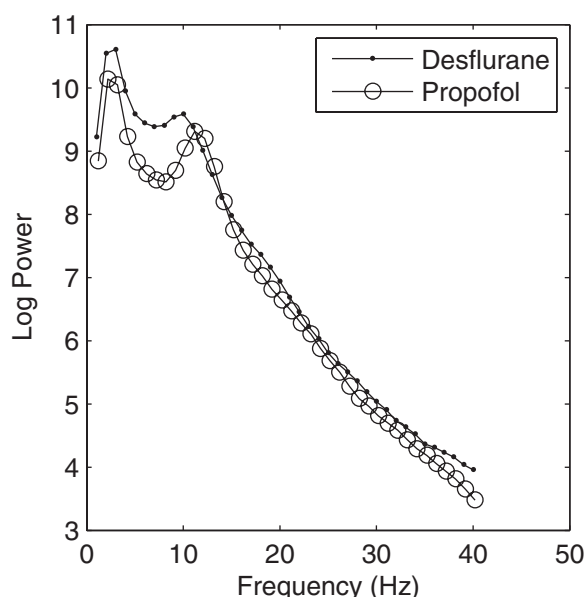


Fig. 4. Mean power spectra of the propofol and desflurane groups at completion of surgical wound closure.

when neurons in thalamocortical networks become hyperpolarized and move to a burst-firing mode.^{19–21} On the other hand, activation of endogenous cholinergic and aminergic neuromodulator systems results in cortical and thalamic neuronal depolarization, which reduces spindle activity in the electroencephalogram.²¹ This might be why scopolamine prevents dream recall after anesthesia.²² Our results suggest that patients who report dreaming lose their spindles in the recovery period to a greater degree than those who do not report dreaming. Whether the reduction in spindles is a direct electroencephalographic manifestation of the dreaming process itself or is an indication of likely improved dream recall cannot be determined from our data. The spindle activity found in stage 2 non-REM sleep is associated with impairment of memory consolidation; hence dreams are more difficult to recall after non-REM than REM sleep.^{4,23} Our results support this idea.

We also found that the patients who reported dreaming had a consistent tendency to show more high-frequency power (20–40 Hz) in their electroencephalogram towards the end of their operation, even when they were still unresponsive. This is consistent with electroencephalographic findings in dreamers during natural sleep⁴ and with the study by Aceto *et al.*,²⁴ which found increased mid-latency cortical evoked potentials during anesthesia in patients who reported dreaming on emergence. Although the contribution of evoked potentials to the raw electroencephalographic signal is small, mid-latency evoked potentials contribute to the 20- to 40-Hz frequency band.

We also observed substantial differences in raw electroencephalographic patterns, but not in BIS values, between the propofol and desflurane groups. Our findings are of interest for two reasons. First, different electroencephalographic patterns for different drugs are a potential source of error in depth-of-anesthesia monitors. Of note, patients in the propofol group opened their eyes at lower BIS values than patients in the desflurane group, suggesting that the relationship between BIS and the clinical level of consciousness is different for the two drugs. Second, the differences in raw electroencephalographic pattern may be an indicator of differences in drug mechanisms of action. The propofol patients had larger and faster spindle-like patterns than the desflurane patients. Although the mechanisms of drug-induced spindles are only partially understood, the most parsimonious explanation is that propofol is a “cleaner” drug than desflurane. Presumably the sleep-spindle-like “oscillatory” electroencephalogram seen in our propofol group is largely the result of the γ -amino-butyric acid (GABA)-ergic actions of propofol, whereas the less well-defined, predominantly slower waves of the electroencephalogram in our desflurane group are caused by the additional (and unknown) receptor and ion-channel effects of volatile anesthetic agents (e.g., potassium channel opening, *N*-methyl-D-aspartate receptor blockade).^{13,14}

Table 7. Raw Electroencephalographic Parameters in Patients Randomized to Desflurane and Propofol

Parameter	Desflurane (n = 75)	Propofol (n = 75)	P Value
Wound closure			
Slope	−0.19 (−0.15 to −0.22)	−0.16 (−0.13 to −0.19)	0.002
Intercept	10.61 (10.47 to 10.80)	9.83 (9.46 to 10.05)	< 0.0001
α Peak	9.85 (9.39 to 10.35)	9.48 (8.86 to 10.17)	0.008
Spindle amplitude	1.09 (0.77 to 1.49)	1.59 (1.20 to 1.96)	< 0.0001
Δ Peak	10.74 (10.26 to 11.18)	10.21 (9.41 to 10.92)	0.001
Mid-surgery			
10.68 Hz spindle	8.63 (6.15 to 12.45)	12.66 (10.05 to 15.84)	< 0.0001
12.82 Hz spindle	5.03 (2.88 to 6.85)	7.83 (6.1 to 10.02)	< 0.0001
16.02 Hz spindle	2.42 (1.67 to 3.47)	3.00 (2.39 to 4.02)	0.02
21.36 Hz spindle	1.05 (0.73 to 1.57)	1.33 (0.99 to 2.04)	0.003
Peak frequency of spindle	10 Hz	11 Hz	< 0.001
Peak frequency of Δ	3 Hz	2 Hz	< 0.001

Results are presented as median (interquartile range). The spindle units are the percentage of electroencephalographic data points that could be associated with a spindle sequence.

Part of our study involved exploring which of the many possible electroencephalographic parameters would maximize the differences between the groups. For this purpose, we used several different analytic approaches (spectral and ordinal). The main problem with this approach is that any observed differences might have arisen by chance and may not be robustly reproducible. This is unlikely in the desflurane-propofol comparison, because the *P* values were very low (≤ 0.001) and because we obtained similar results with different methods of analysis. In the dreamer-nondreamer comparison, the differences were much smaller. However, the changes were consistent over time and consistent with previously published work. We can be sure that our hypothesis that the dreamers might be in a slow-wave sleep state has been disproved.

Another potential limitation of this study is that patients in the propofol group exhibited more apparent variation in anesthetic depth than desflurane patients. This may be explained by the pharmacodynamic plateau effect that is seen in processed electroencephalographic variables with volatile anesthetics but not with propofol.²⁵ In addition, propofol patients received more opioids than patients in the desflurane group. This could have confounded the study because the electroencephalographic effects that we observed in the propofol group resulted from propofol combined with increased doses of opioids. Opioids are not characteristically associated with increased spindle activity in the electroencephalogram, but it is conceivable that their antinociceptive effects contributed to the increased spindle activity observed in the electroencephalograms of those in the propofol group. Finally, we could only obtain usable raw electroencephalographic data from half of the patients. These patients were not significantly different from the patients who were included; nevertheless, the power of our study to find differences between raw electroencephalographic parameters could have been limited. However, we can be confident that our study was adequately powered with respect to finding a difference between the incidence of dreaming in propofol and desflurane patients if one existed.

We conclude that reported dreaming during anesthesia is associated with more high-frequency power and fewer spindles in the electroencephalogram in the 5-min period just before recovery of full cognition. Whether these observations are the result of more actual dreaming mentation or less amnesia for the dreams is unknown.

The authors acknowledge the contributions of Jacklyn De Gabriele, R.N., Research Nurse, Department of Anaesthesia and Pain Management, Royal Mel-

bourne Hospital, Melbourne, Australia; Susan March, R.N., and Shauna Fatovich, R.N., Research Nurses, Royal Perth Hospital; and Desiree Cavill, R.N., and Tracy Bingham, R.N., Research Nurses, King Edward Memorial Hospital for Women, Perth, Australia.

References

1. Leslie K, Skrzypek H, Paech M, Kurowski I, Whybrow T: Dreaming during anesthesia and anesthetic depth in elective surgery patients: A prospective cohort study. *ANESTHESIOLOGY* 2007; 106:33-42
2. Lichter J, Alessi R, Lane B: Sleep tendency as a measure of recovery after drugs used for ambulatory surgery. *ANESTHESIOLOGY* 2002; 96:878-83
3. Franks N: General anaesthesia: From molecular targets to neuronal pathways of sleep and arousal. *Nat Rev Neurosci* 2008; 9:370-86
4. Williamson P, Csima A, Galin H, Mamelak M: Spectral EEG correlates of dream recall. *Biol Psychiatry* 1986; 21:717-23
5. Bertolo H, Paiva T, Pessoa L, Mestre T, Marques R, Santos R: Visual dream content, graphical representation and EEG alpha activity in congenitally blind subjects. *Brain Res Cogn Brain Res* 2003; 15:277-84
6. Hong C, Jin Y, Potkin S, Buchsbaum M, Wu J, Callaghan G, Nudleman K, Gillin J: Language in dreaming and regional EEG alpha power. *Sleep* 1996; 19:232-5
7. Morel C, Hoffmann R, Moffitt A: The electrophysiological correlates of dream recall and nonrecall from stage 2 sleep. *Can J Psych* 1991; 45:140-7
8. Esposito M, Nielsen T, Paquette T: Reduced alpha power associated with the recall of mentation from stage 2 and stage REM sleep. *Psychophysiology* 2004; 41:288-97
9. Marsch S, Schaefer H, Tschan C, Meier B: Dreaming and anaesthesia: Total Iv anaesthesia with propofol *versus* balanced volatile anaesthesia with enflurane. *Eur J Anaesthesiol* 1992; 9:331-3
10. Brandner B, Blagrove M, McCallum G, Bromley L: Dreams, images and emotions associated with propofol anaesthesia. *Anaesthesia* 1997; 52:750-5
11. Kasmacher H, Petermeyer M, Decker C: Incidence and quality of dreaming during anaesthesia with propofol compared with enflurane. *Anaesthetist* 1996; 45:146-53
12. Hellwagner K, Holzer A, Gustorff B, Schroegendorfer K, Greher M, Weindl-mayr-Goettel M, Saletu B, Lackner F: Recollection of dreams after short general anaesthesia: Influence on patient anxiety and satisfaction. *Eur J Anaesthesiol* 2003; 20:282-8
13. Grasshoff C, Drexler B, Rudolph U, Antkowiak B: Anaesthetic drugs: Linking molecular actions to clinical effects *Curr Pharm Des* 2006; 12:3665-79
14. Rudolph U, Antkowiak B: Molecular and neuronal substrates for general anaesthetics. *Nat Rev Neurosci* 2004; 5:709-20
15. Gupta A, Stierer T, Zuckerman R, Sakima N, Parker S, Fleisher L: Comparison of recovery profile after ambulatory anesthesia with propofol, isoflurane, sevoflurane and desflurane: A systematic review. *Anesth Analg* 2004; 98:632-41
16. Luginbühl M, Wuthrich S, Petersen-Felix S, Zbinden A, Schnider T: Different benefit of bispectral index (BIS) in desflurane and propofol anesthesia. *Acta Anaesthesiol Scand* 2003; 47:165-73
17. Brice D, Hetherington R, Utting J: A simple study of awareness and dreaming during anaesthesia. *Br J Anaesth* 1970; 42:535-42
18. Aldrete J, Kroulik D: A postanesthetic recovery score. *Anesth Analg* 1970; 49:924-34
19. Contreras D, Destexhe A, Sejnowski T, Steriade M: Spatiotemporal patterns of spindle oscillations in cortex and thalamus. *J Neurosci* 1997; 17:1179-96
20. Fuentealba P, Timofeev I, Bazhenov M, Sejnowski T, Steriade M: Membrane bistability in thalamic reticular neurons during spindle oscillations *J Neurophys* 2005; 93:294-304
21. Steriade M: Grouping of brain rhythms in corticothalamic systems. *Neuroscience* 2006; 137:1087-106
22. Toscano A, Pancaro C, Peduto V: Scopolamine prevents dreams during general anesthesia. *ANESTHESIOLOGY* 2007; 106:952-5
23. Conduit R, Crewther S, Coleman G: Poor recall of eye-movement signals from Stage 2 compared to REM sleep: Implications for models of dreaming. *Conscious Cogn* 2004; 13:484-500
24. Aceto P, Congedo E, Lai C, Valente A, Gualtieri E: Dreams recall and auditory evoked potentials during propofol anaesthesia. *Neuroreport* 2007; 18: 823-6
25. Kreuer S, Bruhn J, Larsen R, Grundmann U, Shafer S, Wilhelm W: Application of bispectral index and narcotrend index to the measurement of the electroencephalographic effects of isoflurane with and without burst suppression. *ANESTHESIOLOGY* 2004; 101:847-54