

Sleep Disturbances after Posterior Scoliosis Surgery with an Intraoperative Wake-up Test Using Remifentanyl

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Background: The intraoperative wake-up test is a standard procedure for early recognition of neurologic complications after posterior correction of idiopathic scoliosis. In this prospective, single-blinded cohort study, the impact of the wake-up test and the opioid used for anesthesia on the quality of the patients' sleep after scoliosis surgery was investigated up to 12 months postoperatively.

Methods: Patients were classified into three groups: posterior instrumentation with wake-up test using remifentanyl, anterior instrumentation without wake-up test using sufentanil, and posterior instrumentation with wake-up test using sufentanil. The quality of sleep was assessed using the Pittsburgh Sleep Quality Index questionnaire preoperatively as well as 3, 6, and 12 months postoperatively. In addition, data were collected on patients' age, weight, and sex, as well as the duration of the operation and anesthesia, amount of blood loss, specific opioid dosages, and wake-up test times. Statistical analysis was conducted using the Mann–Whitney, Kruskal–Wallis, and Wilcoxon tests.

Results: There were no differences between groups with regard to baseline characteristics. No explicit recall was assessed through all groups. At 3 and 6 months postoperatively, the sleep quality in the posterior–remifentanyl group was significantly poorer than preoperatively and compared with the anterior– and posterior–sufentanil groups. No significant differences in wake-up test times between groups undergoing posterior instrumentation occurred.

Conclusions: This study suggests that patients undergoing scoliosis surgery with an intraoperative wake-up test using remifentanyl had impaired sleep quality that lasted up to 6 months postoperatively. No deterioration in sleep quality was observed with sufentanil. Large randomized trials are now needed to confirm these preliminary results.

INTRAOPERATIVE awareness is one of the major anxieties of patients undergoing surgery.¹ However, patient cooperation is necessary in some types of operative procedures, such as neurosurgery and modern scoliosis repair.² Depending on the type of scoliosis involved, an anterior or posterior correction procedure is chosen. In anterior procedures, correction is performed using convex-side compression, so that there is no danger of distraction paraplegia.³ In contrast, distraction is used in posterior correction spinal fusion, leading to a potential risk of para-

plegia using the latter approach. The correction procedure is therefore performed with strict monitoring of evoked potentials, or with an intraoperative wake-up test subsequent to the correction. The wake-up test in scoliosis surgery was first described by Vauzelle *et al.*⁴ in 1973. At the surgeon's request, the level of the anesthesia is reduced until the patient is able to respond to instructions. Voluntary movement of all extremities allows intraoperative damage to the spinal cord to be either excluded or recognized at an early stage, thus allowing immediate revision in the presence of new-onset neurologic deficits.^{2,5}

Scoliosis surgery represents a special challenge in anesthesia, particularly during the wake-up test. The anesthesiologist has to manage the conflicting situation between sufficient consciousness to prove the patient's voluntary motor function and adequate sedation and analgesia to prevent psychological trauma as a result of postoperative recall. In the past, we noticed that several patients in our department reported sleep disturbances in the ward after scoliosis surgery. Sleep disturbances are experienced as particularly troublesome and can have substantial effects on health and the quality of life.^{6,7}

Because of its short context-sensitive half-life of 3–4 min, the opioid currently recommended in the literature for scoliosis surgery including a wake-up test is remifentanyl.^{5,8–10} However, it still remains unclear whether remifentanyl provides adequate analgesia of the patient during the wake-up test. In addition, the drug itself may impair postoperative sleep.¹¹

We hypothesized that an intraoperative wake-up test and the specific opioid may have an effect on patients' postoperative sleep quality. Therefore, in this prospective, single-blinded cohort study, the impact of the intraoperative wake-up test and the opioid used for anesthesia on patients' sleeping behavior after scoliosis surgery was investigated, including a follow-up evaluation until 1 yr postoperatively.

Materials and Methods

The study was approved by the institutional review board at the University of Muenster, Muenster, Germany (reference number 2008–095-f-S).

The quality of sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The PSQI records seven components of sleep quality, retrospectively over a period of 4 weeks: the frequency of sleep-disturbing events, self-assessment of sleep quality, the

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usual sleeping times, sleep latency and sleep duration, use of sleeping medication, and tiredness during the day. Nineteen self-rated questions, each one scored from 0 to 3, are combined to form seven corresponding component scores, each one ranging from 0 to 3. The global score is generated by summing up all seven component scores and ranges from 0 to 21, with higher values corresponding to reduced sleep quality. There is an empirical cutoff value of 5 that makes it possible to classify patients into "good" and "poor" sleepers. In the first description of the PSQI, healthy individuals who were not awaiting surgery had a PSQI score of 2.67 (± 1.7).^{12,13} The following statistical data are available in the literature on the reliability and validity of the PSQI questionnaire: The stability of the PSQI has been tested in three studies and assessed as satisfactory, with values between 0.82 and 0.89 for the overall PSQI score. The internal consistency and homogeneity of the overall score are 0.77. The sensitivity of the overall PSQI score for various samples of sleep-disturbed patients was always higher than 80% (80–100%), and the specificity was similarly high (83–87%).^{12,14–16} Various studies used the PSQI score in preoperative or postoperative patients before.^{17–19} The PSQI questionnaire is included in the current article as appendix 1, and the scoring instructions are included as appendix 2.

After receiving detailed information and providing written informed consent to participate in the study, the patients completed a PSQI questionnaire preoperatively, as well as 3 months, 6 months, and 1 yr postoperatively. The encoded questionnaires were analyzed by an independent investigator unaware of the study protocol. In addition, data were gathered on patients' age, weight, and sex, as well as on the duration of surgery and anesthesia, the vertebral levels operated on, the amount of blood loss, the opioid used, and its dosage. In addition, the wake-up test times were documented. The patients were also explicitly asked on the first day after the operation whether they had any memory of the wake-up test.

The patients were divided into three groups according to the type of surgery performed and the anesthesiologic standards at our hospital, *i.e.*, posterior instrumentation with an intraoperative wake-up test, using remifentanyl (PR group, $n = 32$), and anterior instrumentation without an intraoperative wake-up test, using sufentanil (anterior group, $n = 40$). After analysis of the initial results, another group with posterior instrumentation, an intraoperative wake-up test, and sufentanil (PS group, $n = 19$) was also investigated.

Anesthesia was performed in all groups in accordance with the following protocol: On the morning of surgery, patients received 0.3 mg/kg midazolam (Hoffmann-La Roche AG, Grenzach-Wyhlen, Germany) orally for premedication. Anesthesia was induced with 5 mg/kg thiopental (Inresa Arzneimittel Ltd., Freiburg, Germany), 0.3 $\mu\text{g}/\text{kg}$ sufentanil (Janssen-Cilag Ltd., Neuss, Germany) in

the anterior and PS groups or 0.5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ remifentanyl (GlaxoSmith Kline Ltd., Munich, Germany) in the PR group, and 0.15 mg/kg cisatracurium (GlaxoSmithKline Ltd.). Anesthesia was maintained using the volatile anesthetic sevoflurane (Abbott Ltd., Wiesbaden, Germany) with an end-tidal concentration of 1.5–3.0 vol% and—depending on the group assignment—intermittent sufentanil administration in the anterior and PS groups or a continuous intravenous infusion of remifentanyl in the PR group (0.2–0.5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). The dosage of each opioid was guided by the patient's individual requirements. The procedure was performed during controlled hypotension (mean arterial pressure 50–65 mmHg) in all groups.²⁰ If necessary, the α -inhibitor urapidil was used to guarantee this range of mean arterial pressure.

The wake-up test was performed in accordance with the following protocol: At the surgeon's request, anesthesia was reduced. In the PR group, the remifentanyl infusion was stopped. Sevoflurane was decreased by stopping the supply and increasing the oxygen flow to 4 l/min in the PR and PS group until spontaneous breathing occurred and the patient followed the instruction to move the extremities. Immediately after the surgical team had checked intact voluntary movement of all extremities, anesthesia was deepened with an intravenous administration of propofol (Fresenius Kabi Ltd., Bad Homburg, Germany; 1–2 mg/kg) and sufentanil (0.3 $\mu\text{g}/\text{kg}$) or remifentanyl (1 $\mu\text{g}/\text{kg}$). In addition, 2–3 mg midazolam was administered intravenously. The wake-up test times were recorded.

After the wake-up test, anesthesia was continued as described above. Postoperatively, the patients were moved to the recovery room and then discharged to the peripheral wards after having met the criteria for discharge, *i.e.*, consciousness, hemodynamic stability, sufficient breathing, as well as unimpaired swallow and cough reflexes. After posterior surgery, patients were mechanically ventilated in the recovery room for 2 more hours. All patients were treated according to the following pain management protocol: 20 mg/kg paracetamol was administered orally four times per day. In addition, 0.2 mg/kg piritramide was administered intravenously every 6 h from day 1 until 3 after surgery. The dosage was reduced to 0.1 mg/kg on the fourth day. Piritramide was stopped at the fifth postoperative day.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows, version 13.0.1 (November 2004; SPSS, Inc., Chicago, IL). Categorical variables are expressed as frequency and percentage, whereas continuous variables and PSQI scores are represented as median and interquartile range [25th percentile; 75th percentile]. Before statistical testing, each continuous variable was analyzed exploratively for its normal distribution (using the Kolmogorov-Smirnov test). The Mann-Whitney test was applied for comparison of nonparametric variables between two study groups. The nonparametric

patients' baseline characteristics and PSQI scores were assessed using the Kruskal-Wallis test. The Friedman signed rank test was used to compare the nonparametric time-dependent variables. The chi-square test was performed for comparison of categorical variables.

Pairwise multiple comparisons after the Friedman and Kruskal-Wallis tests were performed using the Miller "simultaneous statistical inference" procedure.^{21,22} The rank average differences for any pair were compared with the critical constant. The null hypothesis was rejected if the rank average difference of any pair exceeded the critical constant. This meant that the difference between the compared samples was significant. Differences were considered as statistically significant at $P < 0.05$.

Results

There were no differences between groups with regard to age, weight, sex, or wake-up test times (table 1). The duration of surgery and anesthesia was significantly shorter in the anterior group as compared with the posterior groups. The opioid dosage, the number of vertebral levels operated on, and the amount of blood loss were also significantly lower in the anterior group. The patients included in the current study did not report any symptoms or memories of the wake-up test. All of them felt comfortable with the postoperative pain management.

Preoperatively, there were no differences between groups with regard to PSQI values (anterior: 3 [3; 5]; PS: 4 [2; 6]; PR: 4 [3; 5]; $P = 0.828$); median values were

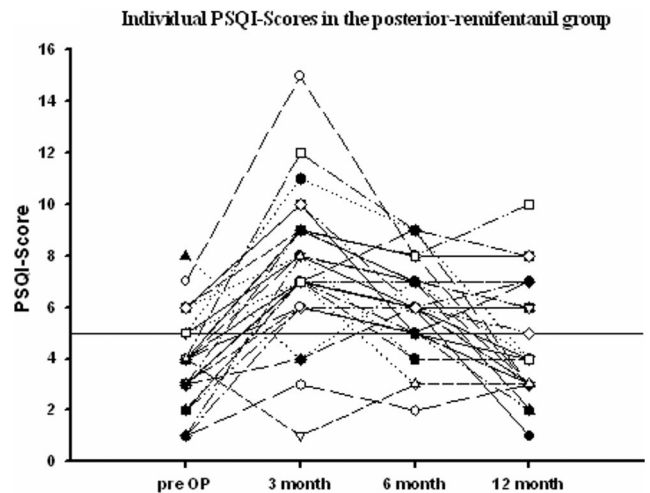


Fig. 1. Individual Pittsburgh Sleep Quality Index (PSQI) scores of all patients included in the group that received posterior instrumentation with wake-up test using remifentanil. The continuous line represents the cutoff value of 5.

below the cutoff value of 5. The patients in the PR group had a significantly diminished quality of sleep up to 6 months postoperatively in comparison with the situation before the surgical procedure ($P < 0.05$). The maximum PSQI value was observed at the first postoperative questionnaire 3 months postoperatively (7 [6.25; 9]). After 1 yr, the PSQI value decreased below the cutoff value of 5 again and thus into the range of the preoperative values (4 [3; 6.75]). The detailed PSQI values for each patient within the PR group are provided in figure 1.

Among the patients in the anterior group, there were no significant differences in sleep quality in comparison with

Table 1. Control Data

	AS	PR	PS	P Value	
Patients, n	40	32	19		
Sex, F/M	36/4	29/3	13/6		0.062§
Age, y	16 [14; 17]	16 [13; 20]	16 [14; 19]		0.336§
Body weight, kg	57 [50; 63]	57 [49; 65]	60 [50; 64]		0.334§
Anesthesia duration, min	303 [266; 325]	345 [305; 400]*	353 [313; 418]†	< 0.000*	0.001† < 0.001§
Operating time, min	190 [170; 220]	240 [210; 295]*	245 [216; 310]†	< 0.000*	0.663‡ < 0.001§
Levels operated on	7 [5; 7]	11 [9; 12]*	11 [9; 12]†	0.000†	0.716‡ < 0.001§
Blood loss, ml	450 [300; 525]	900 [500; 1,288]*	800 [500; 1,050]†	< 0.001*	< 0.001† < 0.001§
Dosage of opioid, $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$	0.006 [0.005; 0.007]	0.275 [0.216; 0.329]*‡	0.006 [0.005; 0.007]	< 0.001*	0.650‡ < 0.001§
Wake-up test times, min	—	7.5 [6.3; 11]	10 [7.6; 13]	0.587†	< 0.001‡ < 0.001§
				< 0.001‡	0.054

Data are presented as median and interquartile range [25th percentile; 75th percentile].

* AS vs. PR. † AS vs. PS. ‡ PR vs. PS. § Overall significance among the three groups.

AS = anterior instrumentation group without wake-up test using sufentanil; PR = posterior instrumentation group with wake-up tests using remifentanil; PS = posterior instrumentation group with wake-up tests using sufentanil.

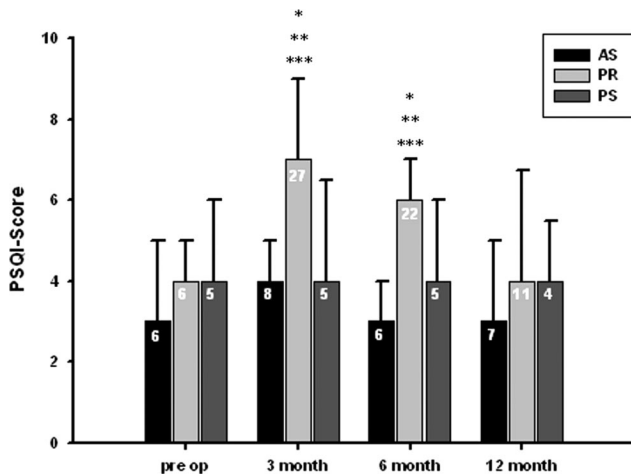


Fig. 2. Comparison of Pittsburgh Sleep Quality Index (PSQI) scores between the groups. Data are presented as median + 75th percentile. Numbers in bars indicate individuals having a PSQI score above 5. AS = anterior instrumentation group without wake-up test using sufentanil; PR = posterior instrumentation with wake-up test using remifentanil; PS = posterior instrumentation with wake-up test using sufentanil. * $P < 0.05$ versus preoperative. ** $P < 0.05$ versus AS group. *** $P < 0.05$ versus PS group.

the baseline values during the entire 1-yr follow-up period. After 3 months, there was a trend toward a slight increase in PSQI values, although they did not increase above the cutoff value of 5 (4 [3; 5]). However, values returned below baseline values after 1 yr (3 [2; 5]). After 3 and 6 months, the PSQI values in the PR group were significantly higher as compared with those in the anterior group ($P < 0.05$).

No significant differences in PSQI values were observed in the PS group during the 1-yr follow-up period compared with preoperative values (4 [2; 6]; $P = 0.772$). The median PSQI score was always below the cutoff value of 5. In comparison with the anterior group, no significant differences in PSQI values were seen at any time point. When the results for the PS group were compared with those for the PR group after 3 and 6 months, PSQI values in the PS group were found to be significantly below those in the PR group ($P < 0.05$). The PSQI scores in the various groups at the individual questionnaire time points are shown in figure 2. Detailed information about the results within the different components of the PSQI questionnaire is presented in appendix 3.

Discussion

The current study demonstrates that patients who have undergone posterior instrumentation spinal fusion with an intraoperative wake-up test using remifentanil slept significantly more poorly up to 6 months postoperatively than did patients with an anterior instrumentation without a wake-up test. Notably, postoperative sleep disturbances after the wake-up test were reduced to values noticed without any wake-up test when sufentanil instead of remifentanil was used for intraoperative analgesia. These

data strongly suggest that not only the wake-up test itself, but also the opioid choice may contribute to postoperative sleep disturbances in patients undergoing scoliosis surgery.

Comparing the results of the anterior and the PR group, the wake-up test may be a cause for the impaired postoperative sleep quality after posterior scoliosis surgery. Therefore, the renunciation of the wake-up test might represent a way of prevention. There are alternative procedures for neurologic monitoring, such as somatosensory evoked potentials and motor evoked potentials.²³ However, the use of these methods is associated with much higher technical effort and costs than the wake-up test.

In addition, the group differences associated with the two different surgical approaches have to be considered. During anterior surgery, the convex side of scoliosis is compressed. In contrast, traction is applied to the dura mater and spinal cord when the vertebral column is distracted during posterior corrective spinal fusion.⁵ This meningeal stress as well as the more severe surgical trauma in the PR group, reflected by an increased blood loss and a higher number of vertebral levels operated on as compared with the anterior surgical procedure (table 1), may also in part be responsible for the postoperative sleep disturbances. However, these theses are only speculative, because no data are available regarding these issues. Because no differences in the PSQI values occurred between the posterior group, which received sufentanil (PS group) instead of remifentanil, and the anterior group at any time point, the wake-up test is probably not the only cause for the diminished postoperative sleep quality in the PR group.

The improved postoperative sleep quality in patients of the PS group compared with the PR group suggests that the choice of opioid may contribute to the patients' postoperative sleep quality, because the two groups differed only in the analgesic agent used. Direct inhibiting effects of central acetylcholine release by opioids can be a cause of sleep disturbances. In this context, it has been reported that opioids, including remifentanil,²⁴ may contribute to a reduction in deep sleep and rapid eye movement sleep.^{25,26} One potential mechanism for this is inhibition of acetylcholine release in the medial pontine reticular formation, contributing to arousal state disruption and impaired memory function.²⁷ However, this effect has been described for morphine and fentanyl, but not for remifentanil.²⁸

Inadequate analgesia during the wake-up test might be another explanation for the poorer sleep observed in the PR group. It is known that despite low-dose remifentanil administration and unaltered hemodynamic parameters, increases in patients' serum epinephrine and norepinephrine concentrations occur during the wake-up test in comparison with the time of the skin incision.²⁹ In addition, remifentanil has a very short, context-sensitive half-life of 3–4 min.³⁰ As a consequence, the opioid is no longer effective shortly after infusion stop for the wake-up test. By contrast, the effective concentration of

sufentanil only declines by half after 33.9 min,¹⁰ suggesting that even after discontinuation of the volatile anesthetic, adequate analgesia was present during the wake-up test in the anterior and PS groups.

In patients of the PR group, pain, which is not remembered explicitly because of the subsequent administration of propofol, midazolam, and remifentanil, might have promoted implicit memory. Andrade and Deeprose⁶ have distinguished between explicit, retrievable, or conscious memory and implicit, nonretrievable, or unconscious memory. An absence of postoperative memory of the wake-up test thus does not exclude intraoperative consciousness.⁶ Implicit memories can trigger sleep disturbances and even posttraumatic stress disorder.³¹ It has been described that despite a lack of hemodynamic changes, some patients recalled colors that had been mentioned during the wake-up test after scoliosis surgery, without having any explicit memories of the wake-up test or the operation.³²

Kress *et al.*³³ recently showed that continuously sedated patients in the intensive care unit had fewer posttraumatic stress disorder symptoms when they received daily "wake-ups." At first glance, this seems to contradict the current results. However, these patients had factual memories of their stay. In contrast, our patients did not have any factual or explicit memories. In this context, the results of Jones *et al.*³⁴ seem to be closer to the patients included in the current study. The authors reported that intensive care patients with delusional memories of their intensive care unit stay were more likely to have posttraumatic stress disorder-related symptoms than were those with factual memories. Because no tests for implicit memory were performed in this study, its influence on patients' postoperative sleep remains uncertain.

The recommendation for remifentanil in anesthetic procedures involving intraoperative wake-up tests is justified by the significant shortening of the arousal time. However, in the studies concerned, either total intravenous anesthesia was used^{5,9} or total intravenous management was compared with volatile anesthesia.⁸ In the current study, no difference in wake-up test times between administration of combined sufentanil and sevoflurane and the combination of sevoflurane and remifentanil occurred.

A major limitation of this study is the lack of assessment of the level of sedation and analgesia during the wake-up test. However, it is a matter of controversy whether an adequate method for monitoring the depth of anesthesia exists currently.^{35,36} The most commonly used method, the Bispectral Index, is also limited by its dependence on external factors such as the anesthetic agents used, the patient's age, the position of the electrodes, and so forth.³⁶ A randomized, controlled, prospective study revealed no lower incidence of awareness with Bispectral Index monitoring (BIS[®]; Aspect Medical Systems, Newton, MA). The authors did not recommend this method as a part of standard practice.³⁷ In fact, there

is not only interindividual but also intraindividual variability in sedation at the same Bispectral Index value.³⁸ Even at a Bispectral Index value of 40, explicit recall is described.³⁹ Monitoring the quality of analgesia also is extremely difficult. The questionnaires were disclosed for practical and ethical reasons, because the patients were intubated and had a large surgical wound at the moment of the wake-up test. Measurement of opioid blood concentrations during the wake-up test would provide only poor evidence, because there is wide interindividual variability in the response to opioids.⁴⁰

Further limitations include the absence of randomization and the later investigation of the PS group. Therefore, evident as well as unknown confounders might have influenced the results. Another point of criticism is that no investigation of an anterior group using remifentanil was performed in the current study. A posterior group without a wake-up test was not investigated, because the alternative technique of evoked potentials is not established at our institution. In addition, it might not be sufficient to disclose explicit recall by asking the patient on the first postoperative day, because explicit recall might occur after several days.⁴¹ However, none of the patients reported having explicit recall afterward. The PSQI scores in this study are lower than those described in other trials (12.0 [10; 16],⁴² 12.5 (\pm 3.8)⁴³). One difference is that this investigation describes long-term effects of one special event, whereas most of the other studies have been concerned with short-term effects or chronic diseases. Furthermore, the patients included in this study were younger and had no primary insomnia or diseases causing sleep disturbances. The administration of midazolam after the wake-up test must be critically questioned, too. More recent research results suggest a dissociated amnesia process for midazolam, *i.e.*, suppression of conscious memory only.⁴⁴ Information that is recorded *via* routes that bypass consciousness can cause negative psychological consequences.⁴⁵

Conclusion

The findings of the current study suggest that the use of remifentanil in posterior scoliosis surgery with an intraoperative wake-up test may result in a higher incidence of postoperative sleep disturbances than the use of sufentanil. However, little is known about the complexity of the interplay between the choice of anesthetic, surgery, intraoperative awareness, and postoperative sleep disturbances. In view of these issues and the current study design, it is only possible to generate hypotheses on the basis of the current data. Further research is needed to determine the interaction between intraoperative wake-up tests and postoperative sleep disturbances in more detail and to clarify whether the choice of opioid affects postoperative sleep quality.

Appendix 1. Pittsburgh Sleep Quality Index (PSQI)

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

- | | |
|---|---------------------------|
| 1. During the past month, when have you usually gone to bed at night? | usual bed time: |
| 2. During the past month, how long (in minutes) has it usually take you to fall asleep each night? | minutes: |
| 3. During the past month, when have you usually gotten up in the morning? | usual getting up time: |
| 4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.) | hours of sleep per night: |

For each of the remaining questions, check the one best response. Please answer *all* questions.

5. During the past month, how often have you had trouble sleeping because you...
- | | |
|--|--|
| a) ... cannot get to sleep within 30 minutes | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| b) ... wake up in the middle of the night or early morning | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| c) ... have to get up to use the bathroom | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| d) ... cannot breathe comfortably? | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| e) ... cough or snore loudly? | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| f) ... feel too cold? | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |
| g) ... feel too hot? | <input type="radio"/> Not during the last month
<input type="radio"/> Less than once a week
<input type="radio"/> Once or twice a week
<input type="radio"/> three or more times a week |

(continued)

Appendix 1. Continued

h) ... had bad dreams?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

i) ... have pain?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

j) ... other reason(s)?

Please describe:

How often during the past month have you had trouble sleeping because of this?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

6. During the past month, how would you rate your sleep quality overall?

Very good
 Fairly good
 Fairly bad
 Very bad

7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all
 Only a very slight problem
 Somewhat of a problem
 A very big problem

10. Do you have a bed partner or roommate?

No bed partner or roommate
 Partner/roommate in other room
 Partner in same room, but not same bed
 Partner in same bed

If you have a roommate or bed partner, ask him/her how often in the past month you have had...

a) loud snoring?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

b) long pauses between breaths while asleep?

Not during the last month
 Less than once a week
 Once or twice a week
 three or more times a week

(continued)

Appendix 1. Continued

c) legs twitching or jerking while you sleep?

- Not during the last month
- Less than once a week
- Once or twice a week
- three or more times a week

d) Episodes of disorientation or confusion during sleep?

- Not during the last month
- Less than once a week
- Once or twice a week
- three or more times a week

e) other restlessness while you sleep?

Please describe:

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Appendix 2. Scoring Instructions for the Pittsburgh Sleep Quality Index:

The Pittsburgh Sleep Quality Index (PSQI) contains 19 self-rated questions and 5 questions rated by the bedpartner or roommate (if one is available). Only self-rated questions are included in the scoring. The 19 self-rated items are combined to form 7 component scores, each of which has a range of 0 to 3. The 7 component scores are then added to yield one "global" score, with a range of 0 to 21.

Scoring proceeds as follows:

Component 1: Self-assessment of sleep quality				
Please score question 6 as described:				
Reply		Score		
„very good“	=	0		
„fairly good“	=	1		
„fairly bad“	=	2		
„very bad“	=	3		
				Component 1: _____

Component 2: Sleep latency				
1. Please score question 2 as described:				
Reply		Score		
≤ 15	=	0		
16-30	=	1		
31-60	=	2		
> 60	=	3		
				Score question 2: _____
2. Please score question 5a as described:				
Reply		Score		
Not during the last month	=	0		
Less than once a week	=	1		
Once or twice a week	=	2		
Three or more times a week	=	3		
				Score question 5a: _____
3. Please sum up the scores of question 2 and question 5a and score as described:				
Sum question 2 + 5a		Score		
0	=	0		
1-2	=	1		
3-4	=	2		
5-6	=	3		
				Component 2: _____

Component 3: Sleep duration				
Please score question 4 as described:				
Reply		Score		
≥ 7h	=	0		
6-7h	=	1		
5-6h	=	2		
< 5h	=	3		
				Component 3: _____

(continued)

Appendix 2. Continued

Component 4: Sleep efficiency			
1. Note the sleep duration in hours (question 4): _____ h			
2. Calculate the hours spent in bed (bed time):			
„get up“-time (Question 3): _____			
“go to bed”time (Question 1): _____			
Number of hours spent in bed: _____ h			
3. Calculate sleep efficiency (ratio of sleeping time and bed time) as described: (sleeping time in h)/(number of hours spent in bed) x 100 = sleep efficiency			
(_____/_____) x 100 = _____ %			
4. Please score component 4 as described:			
Sleep efficiency		Score	
≥ 85	=	0	
75 – 84	=	1	
65 – 74	=	2	
< 65	=	3	
			Component 4: _____

Component 5: Sleep disturbing events			
1. Please score each question from 5b to 5j as described:			
Reply		Score	
Not during the last month	=	0	
Less than once a week	=	1	
Once or twice a week	=	2	
Three or more times a week	=	3	
2. Note the results for question 5b to 5j and sum up the scores:			
5b: _____			
5c: _____			
5d: _____			
5e: _____			
5f: _____			
5g: _____			
5h: _____			
5i: _____			
5j: _____			
sum: _____			
Sum question 5b - 5j		Score	
0	=	0	
1 - 9	=	1	
10 - 18	=	2	
19 - 27	=	3	
			Component 5: _____

(continued)

Appendix 2. Continued

Component 6: Sleep medication				
Please score question 7 as described:				
Reply		Score		
Not during the last month	=	0		
Less than once a week	=	1		
Once or twice a week	=	2		
Three or more times a week	=	3		
				Component 6: _____

Component 7: Tiredness during the day				
1. Please score question 8 as described:				
Reply		Score		
Not during the last month	=	0		
Less than once a week	=	1		
Once or twice a week	=	2		
Three or more times a week	=	3		
				Score question 8: _____
2. Please score question 9 as described:				
Reply		Score		
No problem at all	=	0		
Only a very slight problem	=	1		
Somewhat of a problem	=	2		
A very big problem	=	3		
				Score question 9: _____
3. Please sum up the scores of question 8 and question 9 and score as described:				
Sum question 8 + 9		Score		
0	=	0		
1-2	=	1		
3-4	=	2		
5-6	=	3		
				Component 7: _____

Information: Question 10 is not included into the analysis

Global PSQI score	
Please sum up the 7 component scores = global score	
Component	Score
1. Sleep quality	
2. Sleep latency	
3. Sleep duration	
4. Sleep efficiency	
5. Sleep disturbing events	
6. Sleep medication	
7. Tiredness during the day	
Global score: _____	

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Appendix 3. Scores within Each Component of the Pittsburgh Sleep Quality Index over Time

	Preoperative	3 Months	6 Months	12 Months
Self-assessment of sleep quality				
AS	1.11 (±0.63)	0.91 (±0.70)	0.80 (±0.57)*	0.82 (±0.54)*
PR	0.77 (±0.57)†	1.53 (±0.57)*†‡	1.10 (±0.61)*†	0.97 (±0.61)
PS	0.89 (±0.66)	0.95 (±0.78)	0.89 (±0.81)	0.94 (±0.77)
Sleep latency				
AS	1.23 (±0.94)	1.29 (±0.93)	1.00 (±0.87)	0.94 (±0.86)
PR	1.43 (±0.86)	1.70 (±0.75)†‡	1.43 (±0.63)†	1.20 (±0.96)
PS	0.95 (±1.03)	0.95 (±0.91)	1.11 (±0.74)	0.94 (±0.93)
Sleep duration				
AS	0.09 (±0.51)	0.14 (±0.36)	0.09 (±0.28)	0.14 (±0.42)
PR	0.10 (±0.31)	0.60 (±0.67)*†‡	0.40 (±0.62)*†	0.40 (±0.72)*
PS	0.37 (±0.68)	0.11 (±0.32)	0.21 (±0.54)	0.25 (±0.45)
Sleep efficiency				
AS	0.32 (±0.73)	0.43 (±0.70)	0.31 (±0.47)	0.31 (±0.58)
PR	0.10 (±0.31)‡	1.10 (±0.84)*†‡	0.73 (±0.64)*†‡	0.47 (±0.82)*
PS	0.58 (±0.96)	0.32 (±0.48)	0.21 (±0.42)	0.38 (±0.72)
Sleep-disturbing events				
AS	0.94 (±0.42)	0.97 (±0.30)	0.89 (±0.47)	0.86 (±0.42)
PR	0.97 (±0.49)	1.30 (±0.47)*†	1.20 (±0.41)*†	1.03 (±0.41)
PS	1.00 (±0.58)	1.00 (±0.67)	0.89 (±0.81)	0.88 (±0.81)
Sleep medication				
AS	0.03 (±0.17)	0.00 (±0.00)	0.03 (±0.17)	0.00 (±0.00)
PR	0.03 (±0.18)	0.00 (±0.00)	0.00 (±0.00)	0.10 (±0.40)
PS	0.00 (±0.00)	0.00 (±0.00)	0.05 (±0.23)	0.00 (±0.00)
Tiredness during the day				
AS	0.37 (±0.65)	0.71 (±0.67)*	0.66 (±0.59)*	0.50 (±0.65)
PR	0.50 (±0.86)	1.10 (±0.84)*†§	1.20 (±0.61)*†§	0.67 (±0.61)
PS	0.74 (±0.73)	0.63 (±0.68)	0.58 (±0.61)	1.00 (±0.63)‡

For each category, the score can vary between 0 and 3. Data are presented as mean (±SD).

* $P < 0.05$ vs. preoperative. † $P < 0.05$, AS vs. PR. ‡ $P < 0.05$, AS vs. PS. § $P < 0.05$, PR vs. PS.

AS = anterior instrumentation group without wake-up tests using sufentanil; PR = posterior instrumentation group with wake-up tests using remifentanil; PS = posterior instrumentation group with wake-up tests using sufentanil.

References

- Royston D, Cox F: Anaesthesia: The patient's point of view. *Lancet* 2003; 362:1648-58
- Hall JE, Levine CR, Sudhir KG: Intraoperative awakening to monitor spinal cord function during Harrington instrumentation and spine fusion: Description of procedure and report of three cases. *J Bone Joint Surg Am* 1978; 60:533-6
- Coe JD, Arlet V, Donaldson W, Berven S, Hanson DS, Mudiyan R, Perra JH, Shaffrey CI: Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium: A report of the Scoliosis Research Society Morbidity and Mortality Committee. *Spine* 2006; 31:345-9
- Vauzelle C, Stagnara P, Jouvinroux P: Functional monitoring of spinal cord activity during spinal surgery. *Clin Orthop Relat Res* 1973; 93:173-8
- Rodola F, D'Avolio S, Chierichini A, Vagnoni S, Forte E, Iacobucci T: Wake-up test during major spinal surgery under remifentanil balanced anaesthesia. *Eur Rev Med Pharmacol Sci* 2000; 4:67-70
- Andrade J, Deeprase C: Unconscious memory formation during anaesthesia. *Best Pract Res Clin Anaesthesiol* 2007; 21:385-401
- Benca RM: Consequences of insomnia and its therapies. *J Clin Psychiatry* 2001; 62 (suppl 10):33-8
- Grottke O, Dietrich PJ, Wiegels S, Wappler F: Intraoperative wake-up test and postoperative emergence in patients undergoing spinal surgery: A comparison of intravenous and inhaled anesthetic techniques using short-acting anesthetics. *Anesth Analg* 2004; 99:1521-7
- Imani F, Jafarian A, Hassani V, Khan ZH: Propofol-alfentanil versus propofol-remifentanil for posterior spinal fusion including wake-up test. *Br J Anaesth* 2006; 96:583-6
- Westmoreland CL, Hoke JF, Sebel PS, Hug CC Jr, Muir KT: Pharmacokinetics of remifentanil (G187084B) and its major metabolite (G190291) in patients undergoing elective inpatient surgery. *ANESTHESIOLOGY* 1993; 79:893-903
- Steinmetz J, Holm-Knudsen R, Eriksen K, Marxen D, Rasmussen LS: Quality differences in postoperative sleep between propofol-remifentanil and sevoflurane anaesthesia in infants. *Anesth Analg* 2007; 104:779-83
- Buyse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Res* 1989; 28:193-213
- Gentili A, Weiner DK, Kuchibhatla M, Edinger JD: Test-retest reliability of the Pittsburgh Sleep Quality Index in nursing home residents. *J Am Geriatr Soc* 1995; 43:1317-8
- Wittchen HU, Krause P, Hoyer M, Pittrow D, Winter S, Spiegel B, Hajak G, Riemann D, Steiger A, Pfister H: NISAS-2000: The "Nationwide Insomnia Screening and Awareness Study." Prevalence and interventions in primary care [in German]. *Fortschr Med Orig* 2001; 119:9-19
- Fichtenberg NL, Putnam SH, Mann NR, Zafonte RD, Millard AE: Insomnia screening in postacute traumatic brain injury: Utility and validity of the Pittsburgh Sleep Quality Index. *Am J Phys Med Rehabil* 2001; 80:339-45
- Doi Y, Minowa M, Uchiyama M, Okawa M, Kim K, Shibui K, Kamei Y: Psychometric assessment of subjective sleep quality using the Japanese version of the Pittsburgh Sleep Quality Index (PSQI) in psychiatric disordered and control subjects. *Psychiatry Res* 2000; 97:165-72
- Hedges C, Redeker NS: Comparison of sleep and mood in patients after on-pump and off-pump coronary artery bypass surgery. *Am J Crit Care* 2008; 17:133-40
- Kachuee H, Ameli J, Taheri S, Assari S, Riahipour F, Khedmat H, Saadat AR: Sleep quality and its correlates in renal transplant patients. *Transplant Proc* 2007; 39:1095-7
- Cai T, Gardener N, Abraham L, Boddy V, Abrams P, Bartoletti R: Impact of surgical treatment on nocturia in men with benign prostatic obstruction. *BJU Int* 2006; 98:799-805
- Degoutte CS: Controlled hypotension: A guide to drug choice. *Drugs* 2007; 67:1053-76
- Miller R: Simultaneous Statistical Inference, 2nd edition. New York, Springer, 1981, chapters 6 and 7, pp 165-78
- Sachs LHJ: Utilized Statistics, 12th edition. Berlin, Springer, 2006, chapter 7.5.4, p 445, chapter 7.5.6, p 459
- Schwartz DM, Auerbach JD, Dormans JP, Flynn J, Drummond DS, Bowe JA, Laufer S, Shah SA, Bowen JR, Pizzutillo PD, Jones KJ: Neurophysiological detection of impending spinal cord injury during scoliosis surgery. *J Bone Joint Surg Am* 2007; 89:2440-9
- Bonafide CP, Aucutt-Walter N, Divittore N, King T, Bixler EO, Cronin AJ: Remifentanil inhibits rapid eye movement sleep but not the nocturnal melatonin surge in humans. *ANESTHESIOLOGY* 2008; 108:627-33
- Shaw IR, Lavigne G, Mayer P, Choiniere M: Acute intravenous administra-

- tion of morphine perturbs sleep architecture in healthy pain-free young adults: A preliminary study. *Sleep* 2005; 28:677-82
26. Dimsdale JE, Norman D, DeJardin D, Wallace MS: The effect of opioids on sleep architecture. *J Clin Sleep Med* 2007; 3:33-6
27. Parikh SS, Chung F: Postoperative delirium in the elderly. *Anesth Analg* 1995; 80:1223-32
28. Mortazavi S, Thompson J, Baghdoyan HA, Lydic R: Fentanyl and morphine, but not remifentanyl, inhibit acetylcholine release in pontine regions modulating arousal. *ANESTHESIOLOGY* 1999; 90:1070-7
29. Eroglu A, Solak M, Ozen I, Aynaci O: Stress hormones during the wake-up test in scoliosis surgery. *J Clin Anesth* 2003; 15:15-8
30. Beers R, Camporesi E: Remifentanyl update: Clinical science and utility. *CNS Drugs* 2004; 18:1085-104
31. Sigalovsky N: Awareness under general anesthesia. *AANA J* 2003; 71:373-9
32. McCann ME, Brustowicz RM, Bacsik J, Sullivan L, Auble SG, Laussen PC: The bispectral index and explicit recall during the intraoperative wake-up test for scoliosis surgery. *Anesth Analg* 2002; 94:1474-8
33. Kress JP, Gehlbach B, Lacy M, Pliskin N, Pohlman AS, Hall JB: The long-term psychological effects of daily sedative interruption on critically ill patients. *Am J Respir Crit Care Med* 2003; 168:1457-61
34. Jones C, Griffiths RD, Humphris G, Skirrow PM: Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2001; 29:573-80
35. Kalkman CJ, Drummond JC: Monitors of depth of anesthesia, *quo vadis?* *ANESTHESIOLOGY* 2002; 96:784-7
36. Drummond JC: Monitoring depth of anesthesia: With emphasis on the application of the Bispectral Index and the middle latency auditory evoked response to the prevention of recall. *ANESTHESIOLOGY* 2000; 93:876-82
37. Avidan MS, Zhang L, Burnside BA, Finkel KJ, Searleman AC, Selvidge JA, Saager L, Turner MS, Rao S, Bottros M, Hantler C, Jacobsohn E, Evers AS: Anesthesia Awareness and the Bispectral Index. *N Engl J Med* 2008; 358:1097-108
38. Russell IF, Lerou J: A similar BIS value does not mean a similar depth of anaesthesia. *Br J Anaesth* 2007; 99:592
39. Rampersad SE, Mulroy MF: A case of awareness despite an "adequate depth of anesthesia" as indicated by a bispectral index monitor. *Anesth Analg* 2005; 100:1363-4
40. Lotsch J, Skarke C, Liefhold J, Geisslinger G: Genetic predictors of the clinical response to opioid analgesics: Clinical utility and future perspectives. *Clin Pharmacokinet* 2004; 43:983-1013
41. Sandin RH, Enlund G, Samuelsson P, Lennmarken C: Awareness during anaesthesia: A prospective case study. *Lancet* 2000; 355:707-11
42. Osorio CD, Gallinaro AL, Lorenzi-Filho G, Lage LV: Sleep quality in patients with fibromyalgia using the Pittsburgh Sleep Quality Index. *J Rheumatol* 2006; 33:1863-5
43. Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F: Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. *J Psychosom Res* 2002; 53:737-40
44. Arkhipov VI: Memory dissociation: The approach to the study of retrieval processes. *Behav Brain Res* 1999; 106:39-46
45. Murphy ST, Zajonc RB: Affect, cognition, and awareness: Affective priming with optimal and suboptimal stimulus exposures. *J Pers Soc Psychol* 1993; 64:723-39