

## Sedation during Spinal Anesthesia

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**Background:** Central neuraxial anesthesia has been reported to decrease the dose of both intravenous and inhalational anesthetics needed to reach a defined level of sedation. The mechanism behind this phenomenon is speculated to be decreased afferent stimulation of the reticular activating system. The authors performed a two-part study (nonrandomized pilot study and a subsequent randomized, double-blind, placebo-controlled study) using the Bispectral Index (BIS) monitor to quantify the degree of sedation in unmedicated volunteers undergoing spinal anesthesia.

**Methods:** Twelve volunteers underwent BIS monitoring and observer sedation scoring (Observer's Assessment of Alertness/Sedation Scale [OAA/S]) before and after spinal anesthesia with 50 mg hyperbaric lidocaine, 5%. Subsequently, 16 volunteers blinded to the study were randomized to receive spinal anesthesia with 50 mg hyperbaric lidocaine, 5% (n = 10) or placebo (n = 6) and underwent BIS and OAA/S monitoring.

**Results:** In part I, significant changes in BIS scores of the volunteers occurred progressively ( $P = 0.003$ ). The greatest variations from baseline BIS measurement occurred at 30 and 70 min. In part II, there were significant decreases in OAA/S and self-sedation scores for patients receiving spinal anesthesia versus control patients ( $P = 0.04$  and  $0.01$ , respectively). The greatest decrease in OAA/S scores occurred at 60 min. BIS scores were similar between groups ( $P = 0.4$ ).

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**Conclusions:** Spinal anesthesia is accompanied by significant sedation progressively when compared with controls as measured by OAA/S and self-sedation scores. This effect was not related to block height. The late sedation observed by OAA/S at 60 min may indicate a second mechanism of sedation, such as delayed rostral spread of local anesthetics. BIS was not a sensitive measure of the sedation associated with spinal anesthesia in the randomized, blinded portion of this study. (Key words: Bispectral monitoring; local anesthetics.)

IN 1994, Tverskoy *et al.*<sup>1</sup> reported that subarachnoid bupivacaine decreased the hypnotic requirements of midazolam and thiopental. Subsequent work confirmed these findings and reported decreased anesthetic requirements for patients undergoing epidural or spinal anesthesia and receiving midazolam,<sup>2-3</sup> isoflurane,<sup>4</sup> or sevoflurane.<sup>5</sup> Recently, Gentili *et al.*,<sup>6</sup> using an observer-rated scale of sedation, reported that patients undergoing bupivacaine spinal anesthesia had increasing sedation with increasing block height and hypothesized that decreased cerebral arousal secondary to decreased afferent input from the spinal cord was the mechanism. High-order spectral analysis in the form of bispectral electroencephalography (Bispectral Index [BIS]; Aspect Medical Systems, Natick, MA) has been reported to correlate with or predict levels of sedation in patients or volunteers receiving volatile agents, propofol,<sup>7</sup> midazolam,<sup>8</sup> opioids,<sup>9</sup> or nitrous oxide.<sup>10</sup> The effects of spinal anesthesia alone on cerebral arousal as measured by quantitative electroencephalography parameters has not been reported. Therefore, we sought to test the hypothesis that observed levels of sedation occurring during spinal anesthesia could be quantified by BIS monitoring and correlated with the extent of sensory blockade.

## Materials and Methods

### Part I

After obtaining institutional review board approval, 12 volunteers with American Society of Anesthesiology physical status 1 or 2 consented to undergo baseline bispectral analysis monitoring, 50-mg 5%-lidocaine spinal

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**Table 1. Observer's Assessment of Alertness/Sedation Scale (OAA/S)**

Subscore	Responsiveness	Speech	Facial Expression	Eyes
5	Responds readily to name spoken in normal tone	Normal	Normal	Clear
4	Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed mild ptosis
3	Responds only after name spoken loudly or repeatedly	Slurring or slowing	Marked relaxation	Glazed marked ptosis
2	Responds after mild prodding or shaking	Few recognized words		
1	Does not respond to mild prodding or shaking			

anesthesia without supplemental intravenous sedation, and continuous BIS monitoring. Exclusion criteria included a history of radicular pain, back pain of any type, neurologic or psychiatric disease, or concurrent medications.

To determine baseline BIS measurements, volunteers were placed in a darkened glass room with soft music and left undisturbed for 10 min. The baseline BIS measurement was obtained at the end of this 10-min interval. BIS was measured continuously during this period as well as throughout the study and was recorded every 5 min.

After baseline testing, volunteers received a peripheral intravenous infusion with 6 ml/kg lactated Ringer's solution. Spinal anesthesia was performed with the unседated volunteer in the lateral decubitus position using a 25-gauge Whitacre needle (Kendall Mansfield, MA) with the orifice directed laterally at the L2-L3 interspace. Cerebrospinal fluid (0.2 ml) was aspirated before and after injection of 50 mg plain 5% hyperbaric lidocaine (Astra USA, Westborough, MA). Volunteers were positioned supine for 5 min and then placed in a modified position with pillows underneath the knees. Additional monitoring included electrocardiography, automated blood pressure, and pulse oximetry. Block height and duration as determined by cold discrimination with alcohol swab, as well as Bromage scale of motor block, were assessed every 5 min for the first 30 min and then every 10 min until block resolution. Observer's Assessment of Alertness/Sedation Scale (OAA/S<sup>11</sup>; table 1) was recorded every 5 min during the study. At the conclusion of the study, volunteers were asked to report their perceived degree of sedation on a scale of 1-10 (1 = wide awake, 10 = asleep).

### Part II

After obtaining institutional review board approval, power analysis, and informed consent, 16 volunteers with American Society of Anesthesiologists physical status 1 or 2 consented to undergo baseline BIS monitoring, randomization to a 50-mg 5%-lidocaine spinal anesthesia or placebo without supplemental intravenous sedation,

and continuous BIS monitoring. Exclusion criteria included a history of radicular pain, back pain of any type, neurologic or psychiatric disease, or concurrent medications.

Volunteers received a peripheral intravenous infusion with 6 ml/kg lactated Ringer's solution. Spinal anesthesia was performed with the unседated volunteer in the lateral decubitus position using a 25-gauge Whitacre needle with the orifice directed laterally at the L2-L3 interspace. Volunteers were randomized by sealed envelope. Cerebrospinal fluid (0.2 ml) was aspirated before and after injection of 50 mg 5% hyperbaric lidocaine for volunteers randomized to spinal anesthesia. Volunteers randomized to placebo underwent spinal needle placement and sham injection. After spinal injection, all volunteers were positioned supine in a semi-isolated induction room with low-level lighting. Monitoring included electrocardiography, automated blood pressure, pulse oximetry, and BIS. Block height to alcohol swab was assessed every 15 min until block resolution by the nonblinded investigator who had performed the spinal anesthetic. OAA/S<sup>11</sup> (table 1) was recorded every 10 min during the study by a blinded research assistant. At the conclusion of the study, volunteers were asked to report their perceived degree of sedation during spinal anesthesia on a scale of 1-10 (1 = wide awake, 10 = asleep).

### Statistical Analysis

Power analysis for part II was performed using pilot data from our institution and from previously published data<sup>12</sup> for mean and SD for awake BIS scores ( $92 \pm 3$ ). Adequate power ( $P = 0.05$ ;  $\beta = 0.8$ ) to detect a difference of 5 in BIS scores required six volunteers per group.

Differences in volunteer demographics were analyzed using cross-tabulation and chi-square or a two-tailed unpaired *t* test. BIS scores were compared between times and between groups using one-tailed *t* tests. Repeated-measures analysis of variance was used to test for a difference in the pattern of mean BIS scores over time between treatment groups, using an interaction be-

**Table 2. Demographics**

Part I—Nonrandomized Volunteers (N = 12)		
Age (yr)	36 ± 8	
Weight (kg)	68 ± 14	
Gender (% male)	25	
Part II—Randomized Volunteers (N = 16)		
	Control (N = 6)	Spinal (N = 10)
Age (yr)	38 ± 10	33 ± 10
Weight (kg)	63 ± 7	78 ± 22
Gender (% male)	17	33

tween time and treatment along with the Greenhouse-Geisser adjustment. OAA/S and self-sedation scores were not normally distributed and were compared between treatment groups using one-tailed nonparametric Mann-Whitney tests. Spearman correlation coefficients were calculated between pairs of sedation measures. Statistical significance was defined as  $P = 0.05$ . Results are expressed as actual number of occurrences, percentage and/or mean ± SD for continuous variables.

## Results

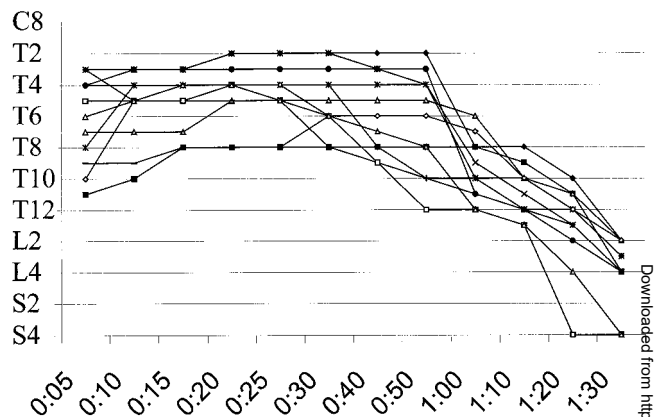
### Part I

The mean age and weight of the volunteers was 35.3 yr and 68.6 kg, respectively (table 2). All volunteers had measurable sensory and motor blockade. Median block height was T4 (fig. 1). All volunteers experienced profound motor block (Bromage score = 3). Mean duration of anesthesia to cold at S2 was 92 min. There were no postdural puncture headaches. No volunteer required treatment for hypotension, bradycardia, or nausea.

**Sedation Scores.** The mean baseline BIS score for volunteers was 96.2. There was a statistically significant change from baseline in the BIS score over time ( $P = 0.003$ ; fig. 2). Three volunteers experienced no significant change from baseline measurements during the study period. The largest deviations in BIS from baseline occurred at 30 and 70 min after the initiation of spinal anesthesia. There was no significant correlation in BIS measurements or OAA/S scores and the level of spinal anesthesia, gender, or age. Median block height at 30 min was T5 and at 70 min was T10. Comparisons of lowest BIS score, OAA/S score, and volunteer-generated self-sedation scores are given in table 3.

### Part II

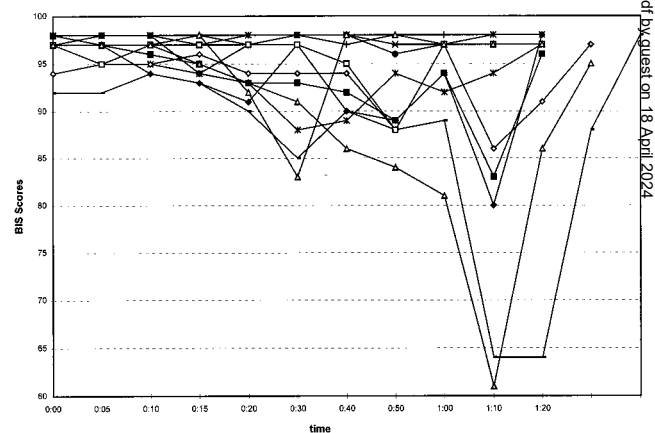
Overall volunteer characteristics were not significantly related to treatment groups or outcomes measures (table



**Fig. 1.** Sensory block level to alcohol swab for each volunteer part I.

2). One volunteer randomized to spinal anesthesia had detectable anesthesia to only the L2 dermatome and was excluded from the final analysis. The placebo group had fewer men and a somewhat lower mean weight and height; however, none of these characteristics differed significantly between the two groups. Median block height was T5 for volunteers receiving spinal lidocaine. Mean duration of sensory analgesia to cold at S2 in volunteers receiving spinal anesthesia was 90 min. There were no postdural puncture headaches. One volunteer required treatment for hypotension and bradycardia. BIS and OAA/S scores were excluded for this volunteer during the period of hypotension.

**Sedation Scores.** Observer's Assessment of Alertness/Sedation Scale and self-sedation scores (figs. 3 and 4) differed significantly between the two groups ( $P = 0.003$  and  $P = 0.01$ , respectively). BIS scores were similar between the two groups across all but three assessments



**Fig. 2.** Bispectral electroencephalogram scores for each volunteer over time ( $P = 0.003$ ), part I.

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**Table 3. Comparison of Sedation Measures—Part I**

Volunteer	Lowest BIS	OAA/S	Self-sedation Score*
1	80	4	7
2	83	5	4
3	61	4	5
4	97	5	1
5	88	5	1
6	91	5	6
7	97	5	8
8	64	4	5
9	97	5	2
10	86	5	4
11	88	5	4
12	83	4	1

\* Scored on a scale of 1–10, where 1 = wide awake, 10 = asleep.

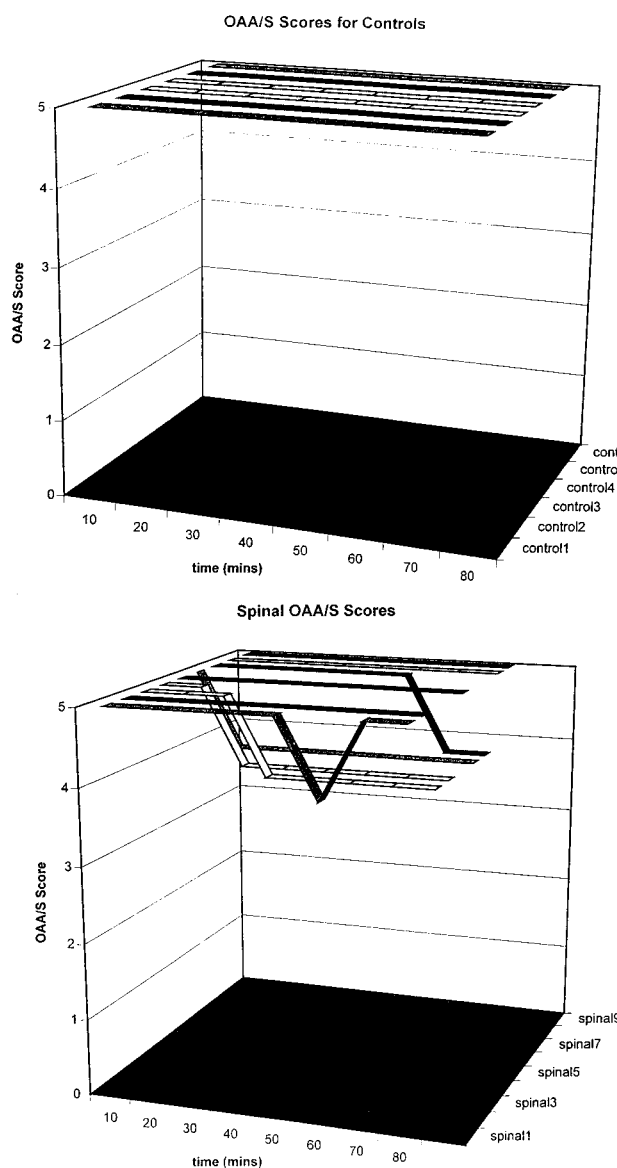
BIS = Bispectral Index; OAA/S = Observer's Assessment of Alertness/Sedation Scale.

times (fig. 5). The mean BIS scores (with the mean taken across all times) were not significantly different between the groups ( $P = 0.4$ ), and the test for a different time pattern between the two groups (an interaction between treatment and time) also was not statistically significant ( $P = 0.4$ ). During 65–75 min, the two groups showed the largest difference in mean scores. However, the treatment differences at each time 65, 70, and 75 min were not statistically significant ( $P = 0.1, 0.3,$  and  $0.07$ , respectively, from a one-tailed  $t$  test unadjusted for multiple comparisons.) Across the 15 volunteers in part II, the mean BIS score had only a very weak correlation (0.2, not significant) with the mean OAA/S score and the self-sedation score. Conversely, the mean OAA/S score and the self-sedation score had a strong correlation (0.7;  $P = 0.002$ , one-sided).

## Discussion

Our results indicate that unmedicated spinal volunteers can have statistically significant changes in their level of consciousness as measured by OAA/S and self-sedation scores over time. These results directly support the findings of investigators who have concluded that both spinal and epidural anesthesia reduce the hypnotic requirements of midazolam,<sup>3</sup> isoflurane,<sup>4</sup> sevoflurane,<sup>5</sup> and thiopental<sup>1</sup> in surgical patients. Two unique findings of this study were that the BIS monitor was not as sensitive an indicator of the sedation associated with spinal anesthesia as was the OAA/S score, and that maximal sedation may have occurred not at the peak of spinal anesthesia but rather at 60 min after spinal injection.

Currently, there are several theories on the cause of sedating effects of neuraxial anesthesia. These include increased systemic levels of local anesthetics,<sup>1,2,4</sup> rostral spread of the local anesthetic with a direct action on the brain,<sup>13</sup> and interruption of spinal afferent input with a decrease in stimulation to the reticular activating system and resultant hypnotic effect.<sup>2,5,13</sup> Two groups of investigators have proven in randomized controlled studies of surgical patients that increased levels of sedation do not appear to be caused by high systemic levels of local



**Fig. 3. Observer's Assessment of Awareness/Sedation Scores, part II. Scores differed significantly between the two groups ( $P = 0.04$ ).**

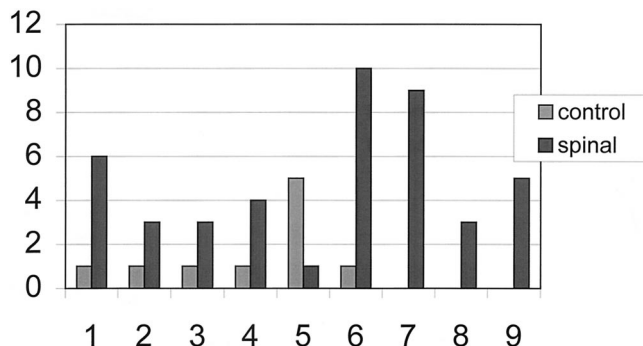


Fig. 4. Self-sedation scores, part II (1 = wide awake, 10 = asleep). Scores differed significantly between the two groups ( $P = 0.01$ ).

anesthetics. Ingaki *et al.*<sup>4</sup> randomized patients to receive normal saline or lidocaine intravenously or epidurally and proved that despite lower systemic levels of lidocaine in the epidural patients, these patients had the lowest requirements of isoflurane for minimum alveolar concentration-awake. Tverskoy *et al.*<sup>2</sup> subsequently studied patients randomized to intramuscular saline or epidural or intramuscular bupivacaine and found that the sedation requirements of intravenous midazolam were lowest in the epidural bupivacaine group. Both groups concluded that increased systemic levels of local anesthetic were probably not responsible for the sedation associated with neuraxial block.

To evaluate the theory that the sedation associated with spinal anesthesia might be secondary to rostral spread and a direct cerebral effect, Eappen and Kissin<sup>13</sup> used an intrathecal rat model. These investigators evaluated the effect of intrathecal bupivacaine on the thiopental doses needed to ablate both hypnotic (eyelid reflex) and nociceptive (withdrawal front digit, corneal reflex) stimulation. They determined that lumbar intrathecal bupivacaine did decrease anesthetic requirements in this model, but that there was no bupivacaine detectable in the brain or cervical spinal cord. Each of these investigators has speculated that the sedation associated with neuraxial anesthesia is caused by decreased spinal afferent input.

In light of published reports, our discovery of peak sedation at 60 min after injection of spinal lidocaine when anesthetic levels are clearly declining is surprising. This finding may indicate that, while early sedation after spinal anesthesia is caused by decreasing afferent spinal input, delayed sedation occurring approximately 1 h after injection of spinal lidocaine may be attributable to an alternate mechanism such as direct rostral spread or

redistribution of blood flow and increasing cerebral concentrations of local anesthetic. Another possible consideration for delayed sedation would be a psychological effect as manifest by the unmedicated volunteer's relief that the study is concluding and the spinal anesthetic level is regressing.

The only other study evaluating sedation in subjects undergoing neuraxial anesthesia without supplemental medication was performed by Gentili *et al.*,<sup>6</sup> who reported increasing sedation in patients with increased levels of spinal anesthesia. There are several important distinctions between our study and that of Gentili *et al.* Gentili's group used a different observer score of sedation (Ramsey score)<sup>14</sup> rather than the OAA/S and BIS and their patients had a higher median spinal level than our volunteers (T2 vs. T4). Additionally, Gentili's group only monitored sedation until 45 min after spinal anesthesia. The decrease in OAA/S score occurring at 60 min in our volunteers appears to be an original observation. If we had monitored for only the first 45 min after spinal anesthesia, our results would also have indicated an increasing degree of sedation associated with block height.

Our study attempted to quantify this previously reported sedation with neuraxial anesthesia by using BIS. The BIS monitor is a signal-processing technology that determines the harmonic and phase relations among the various frequencies measured during electroencephalography.<sup>15</sup> These measurements are then compared with a library of thousands of patients undergoing anesthesia with many different types of anesthetics, and a number from 1 to 100 is generated. This BIS score has been reported to correlate with depth of anesthesia, patient movement,<sup>16</sup> suppression of learning, and level of sedation for propofol,<sup>17,18</sup> midazolam,<sup>8</sup> narcotics,<sup>16</sup> hypnotics,<sup>19</sup> inhalational agents,<sup>9</sup> and nitrous oxide.<sup>10,20</sup> Liu *et al.* reported the changes in BIS and OAA/S for both propofol<sup>7</sup> and midazolam.<sup>8</sup> This group reported that patients with an OAA/S score of 5 (wide awake) had BIS scores of 95-96; patients with an OAA/S score of 3 (responds only after name is spoken loudly or repeatedly) had BIS scores of 86-89, and patients with OAA/S scores of 1 (does not respond to mild prodding or shaking) had average BIS scores of 69-75. Recently, Sleigh *et al.*<sup>12</sup> reported that BIS is a consistent marker for depth of sleep, with light sleep occurring at BIS values of 75-90, slow-wave sleep occurring at BIS values of 20-70, and rapid-eye-movement sleep occurring at BIS values of 75-92.

In this study, unrandomized volunteers undergoing spinal anesthesia did have lower BIS scores than baseline. However, in the double-blind, randomized, placebo-

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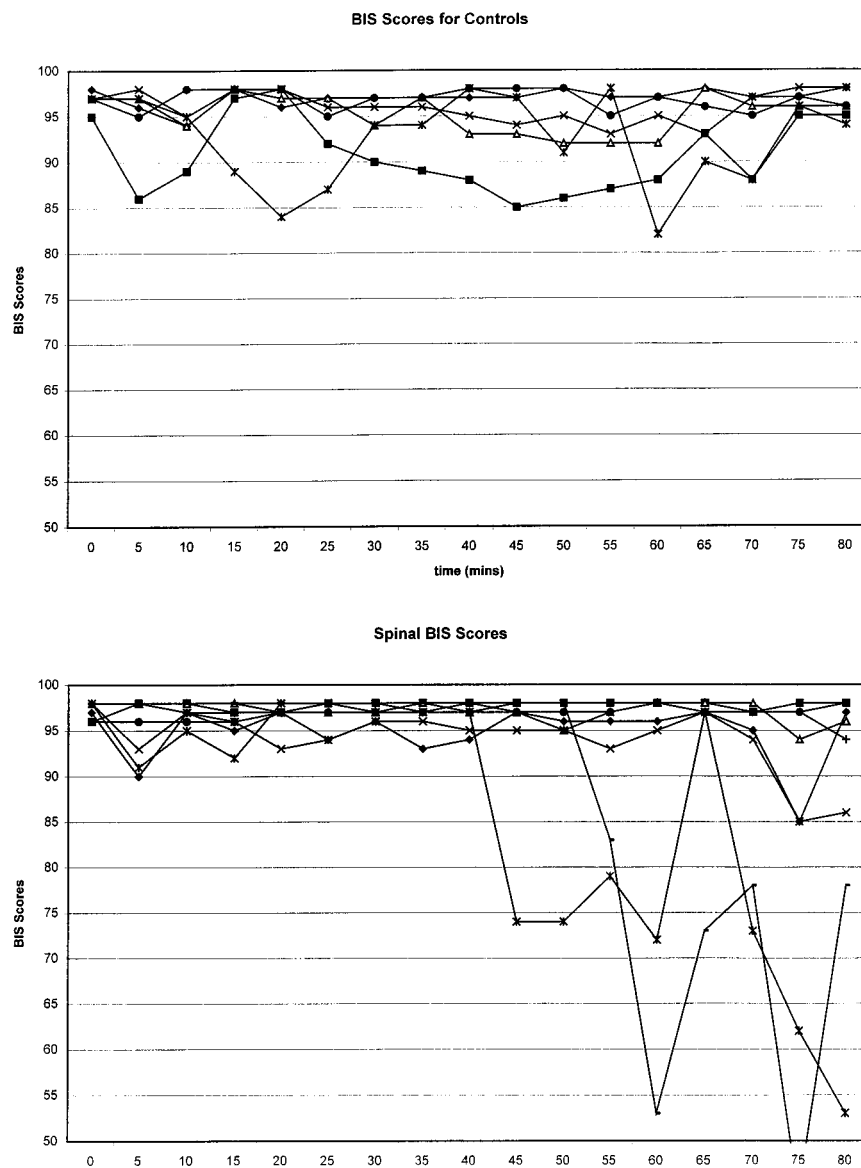


Fig. 5. Bispectral Index scores over time part II. Differences in scores between groups were not statistically significant ( $P = 0.4$ ).

bo-controlled study, these values were not a statistically significant indicator for the sedation associated with spinal anesthesia, although the OAA/S scores were significant indicators. There are several possible explanations for this observation. One explanation is the more rigorously controlled design of the second part of the study. Another possibility is that the degree of sedation associated with spinal anesthesia in unmedicated volunteers is countered by the stimulus of study participation in a busy operating-room setting. In addition, just as patients have variable sensitivities to sedating medications, volunteers may have great variation in susceptibil-

ity to the sedating effects of spinal anesthesia. Finally, perhaps the BIS monitor is simply not a sensitive enough measure of this particular type of sedation. In 1998, Rampil *et al.*<sup>10</sup> reported the results of a study where both BIS and OAA/S scores were monitored during the administration of nitrous oxide to volunteers. Despite concentrations of nitrous oxide of up to 50% and changes in the spectral content of the electroencephalogram, there were no changes in BIS or OAA/S scores in this group of volunteers. Rampil *et al.* concluded that these findings were consistent with the design objective of the BIS monitor as a specific measure of hypnosis. It is possible

that, similar to the effects of 50% nitrous oxide, the sedation/hypnosis associated with spinal anesthesia does not cause enough change in the electroencephalogram to result in a decrease in the BIS number in all volunteers. The significant differences between the phase II spinal and control groups in OAA/S and self-sedation scores is reinforced by the strong and significant correlation between these two measures. The weak and nonsignificant correlation between the BIS score and the other two measures is consistent with the lack of association between BIS and treatment and, again, suggests that BIS is not a particularly sensitive measure of sedation.

There are several limitations to this study design. Despite prestudy power analysis, given the variability in BIS monitoring, 12 and 16 are small sample sizes, and error as a result of inadequate power cannot be disregarded. We attempted to blind both volunteers and observers in part II and to specifically ask the volunteers not to try to determine their group assignment. We also limited the number of times block height was assessed. Despite these efforts, there remains a significant question about whether a volunteer can be truly blinded to having a spinal anesthetic.

In conclusion, this study attempted to quantify a level of sedation in randomized, blinded, volunteers undergoing neuraxial anesthesia using the BIS monitor and OAA/S. Our results are the first to report a statistically significant change over time in unmedicated volunteers undergoing spinal anesthesia compared with controls. In this study, OAA/S was a more sensitive monitor of the sedation occurring with spinal anesthesia than was the BIS monitor. Sedation effects appeared to be most pronounced at 60 min. The finding of substantial sedation 60–70 min after injection of spinal anesthetics have not been reported previously and may indicate an important alternative mechanism of late sedation such as delayed rostral spread of local anesthetics.

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## References

1. Tverskoy M, Shagal M, Finger J, Kissin I: Subarachnoid bupivacaine blockade decreased midazolam and thiopental hypnotic requirements. *J Clin Anesth* 1994; 6:487-90
2. Tverskoy M, Shifrin V, Finger J, Fleyshman G, Kissin I: Effect of epidural bupivacaine block on midazolam hypnotic requirements. *Reg Anesth* 1996; 21:209-13
3. Ben-David B, Vaida S, Gaitini L: The influence of high spinal anesthesia on sensitivity to midazolam sedation. *Anesth Analg* 1995; 81:525-8
4. Inagaki Y, Mashimo T, Kuzukawa A, Tsuda Y, Yoshiya I: Epidural lidocaine delays arousal from isoflurane anesthesia. *Anesth Analg* 1994; 79:368-72
5. Hodgson PS, Liu SS, Gras TW: Does epidural anesthesia have general anesthetic effects? *ANESTHESIOLOGY* 1999; 91:1687-92
6. Gentili M, Chau Huu P, Enel D, Hollande J, Bonnet F: Sedation depends on the level of sensory block induced by spinal anaesthesia. *Br J Anaesth* 1998; 81:970-1
7. Liu J, Singh H, White P: Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. *Anesth Analg* 1997; 84:185-9
8. Liu J, Singh H, White P: Electroencephalogram bispectral analysis predicts the depth of midazolam-induced sedation. *ANESTHESIOLOGY* 1996; 84:64-9
9. Sebel PS, Lang E, Rampil IJ, White PF, Cork R, Jopling M, Smith NT, Glass PSA, Manberg P: A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. *Anesth Analg* 1997; 84:891-9
10. Rampil IJ, Jin-Soo K, Lenhardt R, Negishi C, Sessler DI: Bispectral EEG index during nitrous oxide administration. *ANESTHESIOLOGY* 1998; 89:671-7
11. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, Schwan EM, Siegel JL: Validity and reliability of the Observer's Assessment of Awareness/Sedation Scale: Study with intravenous midazolam. *J Clin Psychopharmacol* 1990; 10:244-51
12. Sleigh JW, Andrzejowski J, Steyn-Ross A, Steyn-Ross M: The bispectral index: A measure of depth of sleep? *Anesth Analg* 1999; 88:659-61
13. Eappen S, Kissin I: Effect of subarachnoid bupivacaine block on anesthetic requirements for thiopental in rats. *ANESTHESIOLOGY* 1998; 88:1036-42
14. Ramsey MAE, Savage TM, Simpson BRJ, Goodwin R: Controlled Sedation with alfaxalone-alfadolone. *Br Med J* 1974; 2:656-9
15. Rampil IJ: A primer for EEG signal processing in anesthesia. *ANESTHESIOLOGY* 1998; 89:980-1002
16. Vernon JM, Lang E, Sebel PS, Manberg P: Prediction of movement using bispectral electroencephalographic analysis during propofol/alfentanil or isoflurane/alfentanil anesthesia. *Anesth Analg* 1995; 80:780-5
17. Kearse LA, Manberg P, Chamoun N, deBros F, Zaslavsky A: Bispectral analysis of the electroencephalogram correlates with patient movement to skin incision during propofol/nitrous oxide anesthesia. *ANESTHESIOLOGY* 1994; 81:1365-70
18. Leslie K, Sessler DI, Schroeder M, Walters K: Propofol blood concentration and the bispectral index predict suppression of learning during propofol/epidural anesthesia in volunteers. *Anesth Analg* 1995; 81:1269-74
19. Flaishon R, Windsor A, Sigl J, Sebel PS: Recovery of consciousness after thiopental or propofol. *ANESTHESIOLOGY* 1997; 86:613-9
20. Leslie K, Sessler DI, Smith WD, Larson MD, Ozaki M, Blanchard D, Crankshaw DP: Prediction of movement during propofol/nitrous oxide anesthesia. *ANESTHESIOLOGY* 1996; 84:52-63