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Hypnotic Depth and the Incidence of Emergence Agitation and Negative Postoperative Behavioral Changes

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Abstract

Background—Emergence agitation (EA) and negative postoperative behavioral changes (NPOBC) are common in children, though the etiology remains unclear. We investigated whether longer times under deep hypnosis as measured by Bispectral Index™ (BIS) monitoring would positively correlate with a greater incidence of EA in the post anesthesia care unit (PACU) and a greater occurrence of NPOBC in children after discharge.

Methods—We enrolled 400 children, ages 1–12 years old, scheduled for dental procedures under general anesthesia. All children were induced with high concentration sevoflurane and BIS monitoring was continuous from induction through recovery in the PACU. A BIS reading <45 was considered deep hypnosis. The presence of EA was assessed in the PACU using the Pediatric Anesthesia Emergence Delirium Scale (PAED). NPOBC were assessed using the Post-Hospital Behavior Questionnaire (PHBQ), completed by parents 3–5 days post-operatively. Data were analyzed using logistic regression, with a $p < 0.05$ considered statistically significant.

Results—The incidence of EA was 27% (99/369) and the incidence of NPOBC was 8.8% (28/318). No significant differences in the incidence of EA or NPOBC were seen with respect to length of time under deep hypnosis as measured by a BIS value of less than 45.

Conclusion—Our data revealed no significant correlation between the length of time under deep hypnosis (BIS < 45) and the incidence of EA or NPOBC. Within this population, these behavioral disturbances do not appear to be related to the length of time under a deep hypnotic state as measured by the BIS.

Keywords

Emergence Agitation; Negative postoperative behavioral changes; hypnotic depth; BIS

INTRODUCTION

Emergence agitation (EA) in pediatric patients is a clinical entity generally defined by behaviors including combativeness, excitation, disorientation and inconsolability (1). The incidence of EA is wide ranging in the literature from 10–80% (2–6). It is usually a self-limited phenomenon, but can be severe and present dangers to both patients and caregivers. Additionally, the severity and duration of EA may demand additional postoperative care personnel, delay parental presence in the Post Anesthesia Care Unit (PACU), and increase time to discharge.

Several factors have been associated with an increased risk of EA including the child's baseline temperament and anxiety levels (7, 8), sevoflurane anesthesia (2, 6, 9, 10), young age (3, 8, 11) and ENT procedures (5). Pain has also been implicated as a factor in EA, but it can be especially difficult to distinguish between pain and EA in the PACU (6, 7, 11). While a multitude of studies have described the incidence and factors associated with EA, its etiology remains unclear.

Following discharge to home, another perioperative complication which has been seen in up to 50% of children postoperatively is the development of negative postoperative behavioral changes (NPOBC) (12). These behaviors include generalized anxiety, nighttime crying, enuresis, separation anxiety and temper tantrums. The incidence of these maladaptive behaviors was also seen in one study to be linked to the incidence of EA seen in the PACU (7). As with EA, several factors have been associated with NPOBC including young age, preoperative anxiety in children and parents, and anesthetic agents such as sevoflurane (12–15). As with EA, the etiology remains unclear.

While the pathogenesis of postoperative behavioral disturbances such as EA and NPOBC remains undefined, we know that ENT procedures such as myringotomy and tympanostomy are associated with a higher incidence of EA (4). This is usually an ultra-short procedure, but is performed using very deep levels of anesthesia. Within adults, titration of BIS levels improves postoperative (16) recovery while longer duration of anesthesia has been seen to be related to early postoperative cognitive dysfunction (17, 18). To our knowledge, no studies have looked at the relationship between hypnotic depth or duration of anesthesia and the incidence of EA or NPOBC in children. We wished to perform an observational study to investigate whether the length of time under deep hypnosis as measured by a BIS monitor reading of <45 is associated with an increased incidence of EA in a population of pediatric dental patients. We hypothesize that longer times under deep hypnosis will be associated with a greater incidence of EA in the PACU. Secondly, we wish to investigate whether length of time under deep hypnosis as measured by a BIS reading of <45 is associated with an increased incidence of NPOBC within this cohort after discharge to home.

METHODS

Following IRB approval, informed consent/assent was obtained for enrollment of 400 ASA I–III children between the ages of 1 and 12 years old. All patients were scheduled for outpatient dental procedures under general anesthesia. Exclusion criteria included pre-existing neurological disorders (e.g. seizure history, developmental delay, psychiatric diagnosis), planned use of ketamine and use of total intravenous anesthesia (TIVA). We also excluded non-English speaking patients to prevent difficulty in obtaining follow up results for NPOBC.

All patients scheduled for outpatient dental procedures meeting inclusion/exclusion criteria during the study period were considered for participation. Following enrollment, a designated study nurse administered the modified Yale Preoperative Anxiety Scale (m-YPAS) (19) prior to the administration of pre-medication. A BIS monitoring strip was then placed on the child's forehead in the preoperative holding area and data collection was begun. BIS data collection was continuous from the pre-operative period through recovery in the PACU. A BIS range from 40–60 is considered general anesthesia. Studies in children have found BIS to correlate with clinical indicators of anesthesia and with the concentration of inhalational agents similar to that seen in adults (20, 21). For this study, we considered a BIS reading of less than 45 to be deep hypnosis (22).

All children were induced with high concentration sevoflurane (6–8%) and nitrous oxide, and maintained on inhalational agent for the case. The choice of maintenance inhalational agent, as well as adjunctive medications given during the case, was determined by the anesthesiologist responsible for care. The anesthesiologist caring for the patient was blinded to the BIS.

The presence of EA was assessed in the PACU by recovery nurses using the Post Anesthesia Emergence Delirium scale (PAED) (Appendix 1) (23). EA was assessed continuously in the PACU from arrival through 10 minutes after the patient had awakened and remained awake. The final score was determined to be the point at which the greatest agitation had occurred. Possible scores ranged from 0–25, with a higher score indicating greater symptoms of EA. Developers of this scale determined a score of 10 to be a reliable cutoff in assessing EA (23). We therefore considered a score of 10 or greater to indicate the presence of EA, and dichotomized results into “yes” or “no” classifications. If EA was present, the type and amount of medication used to treat the patient was recorded, as well as the time required for assistance from additional personnel. Times in the PACU, including time to discharge to phase 2 and time to discharge to home were also documented.

The presence of NPOBC was assessed using the Post Hospital Behavior Questionnaire (PHBQ) (15). This instrument was developed in 1966 to evaluate negative behavioral changes in children following surgery, and has been widely used to assess behavioral changes following hospitalization and procedures, with good test-retest reliability. It is a parent-rated scale, including 27 items in 6 categories of symptoms, that children have been observed to experience post-operatively. The PHBQ was administered by the parents on post-operative day 3–5 and the data was collected via a follow-up phone call. Scoring of the PHBQ occurs on a Likert scale, with a response of 4 or 5 for an item considered to be a negative behavioral change (Appendix 2). The presence of 7 or more negative behavioral changes on the PHBQ was considered positive for NPOBC and the occurrence of NPOBC was dichotomized into the classifications of “yes” or “no” (24).

The primary outcome measure was assessing the relationship between length of time under deep hypnosis and the incidence of EA in the PACU. Secondary outcome measures included assessing the relationship between length of time under deep hypnosis and the incidence of NPOBC following discharge to home, as well as the influence of age, gender, preoperative anxiety and the type of maintenance inhalational agent used on the incidence of EA or NPOBC. We also assessed the relationship between EA and NPOBC, whether length of time in the PACU until discharge to home was increased with the presence of EA, and whether an increased level of care was necessary if EA was present.

To measure the length of time under deep hypnosis, average BIS data points were acquired every minute and were recorded continuously during the study. The data was then downloaded to a secure laptop computer and imported into an excel file for data manipulation. To calculate the length of time with BIS <45, we first deleted all data points with a signal quality average less than 50 or an EMG signal greater than 50. This was to minimize the presence of potential artifact due to poor signal or motion. The following algorithm was then applied. The length of all consecutive time intervals was determined. Then, the sum of the entire length of the interval (one minute) was used if the BIS was less than 45 at both the beginning and end of the interval, but only half the length of the interval (30 seconds) was summed if the BIS was less than 45 on only one side of the interval.

No similar studies were available to allow power analysis for this study. We therefore calculated our sample size using the number of dental procedures performed the previous year at The Children’s Hospital and assumed an expected incidence of EA to be 25%. By

this method, a sample size of 400 would have 80% power to detect statistical significance at the 5% level if the odds ratio was 1.38 for one standard deviation increase in the time under deep hypnosis for logistic regression.

Two sample t-test, chi square test and simple logistic regression were used in univariate analyses comparing EA with non-EA patients or NPOBC with non-NPOBC patients.

RESULTS

Four hundred children were enrolled into this observational study. Final analyses of EA included 369 eligible children, while the final data set for analyses of NPOBC included 318 eligible children. Enrollment data and patient demographics are summarized in Figure 1 and Table 2.

Emergence agitation

After the presence of EA was dichotomized into yes/no results according to the PAED score, analyses revealed the incidence of EA in this population to be 27% (99/369) (95% CI 22%–32%). Logistic regression showed no association between length of time under deep hypnosis and the incidence of EA ($p = 0.6824$) (Table 1).

In our secondary analyses, patients with EA were found to be an average of 0.3 years younger than those who did not experience EA. This difference, however, was not statistically significant ($p = 0.11$). Likewise, logistic regression analysis revealed no significant effect of gender ($p = 0.14$) or preoperative anxiety as assessed by the m-YPAS ($p = 0.31$) on the incidence of EA. There was, however a statistically significant difference in the incidence of EA when examining the inhalational agents used for maintenance of anesthesia. The incidence of EA was significantly greater in those patients maintained on desflurane as compared to those maintained on isoflurane ($p = 0.006$). We found no significant difference in the incidence of EA between patients maintained on desflurane versus sevoflurane, or isoflurane versus sevoflurane (Figure 2).

In terms of the impact of EA in the PACU, there was an increase in care requirements for children who experienced EA. In addition to the primary nurse caregiver, extra PACU personnel were required for care in 49% of patients with EA as opposed to only 15% of those not experiencing EA ($p < 0.001$). The average length of time additional personnel was required when EA was present was 0.2 hours, as opposed to 0.13 hours if EA was not present. Despite this, there was not a significant difference in the length of time patients spent in the PACU until discharge to phase 2 recovery whether or not patients experienced EA ($p = 0.92$). The average length of PACU stay was 0.71 hours whether or not EA was present.

Negative Post Operative Behavioral Changes

After the presence of NPOBC was dichotomized into yes/no categories, analyses revealed the incidence of NPOBC in our study populations to be 8.8% (28/318) (95% CI 5.9%–12.5%). As with EA, logistic regression revealed no significant difference in the incidence of NPOBC with respect to length of time under deep hypnosis ($p = 0.29$) (Table 1).

Secondary analyses included assessing the impact of age, gender, preoperative anxiety, and type of maintenance inhalational agent on the incidence of NPOBC. While patients with NPOBC were, on average, 0.3 years younger than those without NPOBC, there was no statistically significant difference when considering age ($p = 0.48$). Likewise, gender ($p = 0.33$) and preoperative anxiety levels ($p = 0.37$) revealed no significant difference on the incidence of NPOBC. There was an observed increase of about 10% in the incidence of

NPOBC when sevoflurane as opposed to desflurane or isoflurane was used for maintenance of anesthesia. This difference was not statistically significant by chi square analysis ($p = 0.21$). In addition, while we found patients with EA were 3% more likely to have NPOBC, there was not a statistically significant correlation between these two phenomena.

DISCUSSION

We conducted this observational study to determine whether length of time under a deep hypnotic state, as assessed by a BIS monitor reading of less than 45, was associated with the presence of EA in the PACU or NPOBC upon discharge to home. We hypothesized longer times under deep hypnosis would correlate with the occurrence of these postoperative maladaptive behaviors. Within this population of pediatric dental patients, our results found no association between length of time under deep hypnosis and either the incidence of EA in the PACU, or NPOBC upon discharge.

Emergence Agitation

The reported incidence of EA in the literature is variable (2–6). This is likely due to factors including different study populations, confounding factors such as pain, and importantly, the use of various subjective tools to assess the presence of EA. For this study, we used a recently developed and validated scale, the PAED, to assess EA. Using this tool, we found no association between length of time under deep hypnosis and the incidence of EA within this population of pediatric dental patients. Additionally, we found no difference in the incidence of EA when length of time under deep hypnosis was stratified (e.g. <30 minutes, 30–40 minutes, etc.) which might reveal a BIS threshold for EA. Finally, there was no association of higher PAED scores with greater length of time under deep hypnosis.

Several additional factors have been associated with the occurrence of EA including age, baseline temperament and anxiety levels in the child, and sevoflurane anesthesia. Aono et al found preschool age boys seemed to have a higher incidence of EA (11). Our secondary analyses found no effect of age or gender within this study group. Aono's study, however, did not use the PAED to assess EA. They also looked at the occurrence of EA after sevoflurane versus halothane anesthesia. Within the current study, the majority of children received either isoflurane or desflurane as their maintenance agent. The majority of the children in this study were also within the 2–5 year old age range, and it may be that there were not enough children outside this age range to get an accurate picture of age effect on the incidence of EA.

Baseline temperament and anxiety levels in children have been seen to be associated with the occurrence of EA (7, 25). Increased anxiety in the preoperative holding area as well as on induction of anesthesia have been associated with the development of maladaptive behaviors in the postoperative period (7, 26, 27). We used the m-YPAS to assess baseline anxiety levels in children in the preoperative holding area. Our analyses found no correlation between pre-operative anxiety levels and the occurrence of EA in the PACU. A confounding factor, however, may be the near universal use of midazolam pre-medication in our study participants. Prior studies have shown conflicting results regarding the effects of midazolam premedication on emergence behavior, including no effect (28), an increased incidence (29), or a decreased incidence (30) of EA. While these results are inconsistent, it is difficult to compare results of one study to another due to differences in patient population and the tools used to measure EA. We assessed patients prior to the administration of premedication and it is possible that subsequent midazolam may have affected the relationship between the assessed level of preoperative anxiety and the occurrence of EA in the PACU.

Several studies have looked at the effects of the different inhalational agents on the occurrence of EA (2, 6, 9, 31–34). In general, the less soluble agents, sevoflurane and desflurane, have been associated with a higher risk for EA than soluble inhalational agents such as halothane. For this study, all children were induced with sevoflurane and nitrous oxide. The maintenance agent used was then determined by the anesthesiologist caring for the child. Secondary analyses on inhalational agents within our study population found an increased incidence of EA with desflurane as compared to isoflurane. However, we found no difference in the incidence of EA with sevoflurane as compared to either desflurane or isoflurane (Figure 2). Recently, sevoflurane has been reported to produce more behavioral problems on emergence from anesthesia than isoflurane (31). While our data did not find this, the number of children present in the sevoflurane maintenance group in our study was small (n=31), and may not have been large enough to show significance.

EA is defined as a self-limited phenomenon, but may still have physical, psychological and financial impacts in the PACU. Potential harm to patients and post anesthesia care personnel may exist due to the combativeness and disorientation of EA. The severity and duration of EA may also require the additional assistance of postoperative care personnel and delay discharge from the PACU. For children experiencing EA, we found a significant increase in nursing care requirements compared to those that did not. We documented that extra help was required for 37 patients with EA and 29 patients without EA. Within our institution, the average cost of nursing care in the PACU is \$29.29/hour. This equates to an average extra cost of \$5.86 or \$3.80 for each additional nursing provider required to care for children with and without EA, respectively. This cost can accumulate rapidly when more than one additional nurse provider is required due to the presence of EA. For the children involved in this study group, the presence of EA produced a 50% greater cost in PACU nursing care when extra personnel were required. Interestingly, we found no difference in time to discharge to phase 2 care, or to home, regardless of whether or not EA was present.

Negative Post Operative Behavioral Changes

As with EA, the length of time under deep hypnosis, as measured by a BIS value of <45, was not a significant predictor for the occurrence of NPOBC within this population of pediatric dental patients. In addition, the incidence of NPOBC did not change when length of time under deep hypnosis was stratified and there was no association between increasing PHBQ scores and increasing length of time under deep hypnosis.

NPOBC has been associated with several factors including young age, increased anxiety in the preoperative and induction periods, and type of inhalational anesthetic agent used (12–15, 35). Within this population of pediatric dental patients we found there to be no association with age, gender or type of maintenance inhalational agent used, and the incidence of NPOBC. Kain et al. observed an association between preoperative anxiety and the occurrence of NPOBC, as well as an association between the occurrence of EA in the PACU and the development of NPOBC on discharge to home (7). Within our study population we discovered no difference in the occurrence of NPOBC on follow-up 3–5 days postoperatively regardless of pre-operative anxiety levels. There was also no association between the occurrence of EA in the PACU and NPOBC on discharge to home. These results may reflect differences in the study populations, tools used to assess EA, or the use of premedication.

Criticisms of Study

Several criticisms of this study may be raised. First, as an observational study, we did not attempt to control the anesthetic regimen. Though induction with high dose sevoflurane was universal, the choice of maintenance and adjunctive agents used was at the discretion of the

anesthesiologist responsible for the care of the patient. Three dental anesthesiologists at TCH were responsible for the care of the majority of patients in this study (72%). By self reports prior to beginning the study, their techniques were very similar. However, variation did exist which may impact the results of this study. Specifically, bias may have been introduced if the anesthesiologist was anticipating EA in their patient and designed their anesthetic regimen to minimize the occurrence of this phenomenon. To address the issue of maintenance agents being chosen non-randomly by the anesthesiologists in our study, we performed subgroup analyses stratifying by the type of maintenance agent used. We found no significant difference between length of time under deep hypnosis and the occurrence of either EA or NPOBC (Table 3).

Second, the constraints of our system led to multiple assessors of EA in the PACU which may affect the incidence of EA and confound results. To minimize the effects of multiple scorers, we tested for inter-rater reliability quarterly during the study by having the individual responsible for training the PACU nurses administer the PAED scale to patients independently of the nursing staff. Scores were compared and seen to fall within 10% of one another.

Third, a variety of dental procedures were performed including cleanings, crowns, pulpotomies and extractions. Some of these procedures may have produced more pain than others. Pain has been implicated as a factor in EA and can be especially difficult to distinguish from EA in the PACU (7). We attempted to minimize the potentially confounding effects of pain on the assessment of EA by using the PAED scale to evaluate children in the PACU. This scale was developed and validated, including items which assess disturbances in consciousness and cognition to help differentiate pain from EA. Our aim in using this scale was to minimize the effect of pain on behavioral disturbances in the PACU that may affect the incidence of EA in our study.

Finally, another factor that might affect outcomes was the use of midazolam pre-medication. Eighty nine percent of our study participants received a midazolam premedication. The incidence of EA was 27% in those patients receiving midazolam and 23% in those who did not receive a premedication ($p = 0.5$). For NPOBC, the incidence of behavioral changes was seen in 9% versus 6%, respectively, of those patients receiving or not receiving midazolam preoperatively ($p = 0.49$). Subgroup analyses were performed and found no significant association between the length of time under deep hypnosis and the occurrence of either EA or NPOBC, regardless of premedication (Table 4). While we observed no correlation between the use of preoperative midazolam and the occurrence of EA or NPOBC with respect to duration of deep hypnosis, this may still be a confounding factor as previously discussed.

In conclusion, our study found that the length of time under a deep hypnotic state appears to be neither predictive nor related to the incidence of EA or NPOBC in this population of children undergoing dental procedures with general anesthesia. The etiology of EA and NPOBC is likely multifactorial and warrants further investigation into factors that may be contributing to these phenomena.

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Appendix 1: Pediatric Anesthesia Emergence Delirium Scale

1. Makes eye contact with caregiver
2. Actions are purposeful
3. Child is aware of surroundings
4. Child is restless
5. Child is inconsolable

Appendix 1: Pediatric Anesthesia Emergence Delirium Scale. Patients were evaluated using the PAED scale developed by Sikich and Lerman (23). Items 1, 2, and 3 are scored: 4 = not

at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Items 4 and 5 are scored: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely. Patients may score from 0–25 with higher scores indicating greater symptoms of EA.

Appendix 2: Post Hospital Behavior Questionnaire

1. Does your child make a fuss about going to bed at night?
2. Does your child make a fuss about eating?
3. Does your child spend time just sitting or lying and doing nothing?
4. Does your child need a pacifier?
5. Does your child seem to be afraid of leaving the house with you?
6. Is your child uninterested in what goes on around him/her?
7. Does your child wet the bed at night?
8. Does your child bet his/her finger nails?
9. Does your child get upset when you leave him/her alone for a few minutes?
10. Does your child need a lot of help doing things?
11. Is it difficult to get your child interested in doing things (playing games, with toys, etc)?
12. Does your child seem to avoid or be afraid of new things?
13. Does your child have difficulty making up his/her mind?
14. Does your child have temper tantrums?
15. Is it difficult to get your child to talk to you?
16. Does your child seem to get upset when someone mentions doctors or hospitals?
17. Does your child follow you everywhere around the house
18. Does your child spend time trying to get or hold you attentions?
19. Is your child afraid of the dark?
20. Does your child have bad dreams at night or wake up and cry?
21. Is your child irregular in his/her bowel movements?
22. Does you child have trouble getting to sleep at night?
23. Does your child seem to be shy or afraid around strangers?
24. Does your child have a poor appetite?
25. Does your child tend to disobey you?
26. Does your child break toys or other objects?
27. Does your child suck his/her fingers or thumb?

Appendix 2: Post Hospital Behavior Questionnaire. The PHBQ, as developed by Vernon et al. in 1966 (15), was used to evaluate negative post operative behavioral changes in the first 3–5 days post-operatively. Items are scored as: 1 = much less than before, 2 = less than before, 3 = same as before, 4 = more than before, 5 = much more than before. If a behavior was not present before or after (i.e. thumb sucking) it was rated as 'same as before'.

Figure 1.

Enrollment Data. A total of 400 children were enrolled. Of these 400 subjects, 30 were excluded due to unanticipated protocol violations (e.g. use of TIVA), technical problems (e.g. failure of the BIS to record properly), or patient request. Of the remaining 370 eligible children, one had no data available for EA analysis and 52 were lost to follow-up for the PHBQ.

Figure 2.

EA vs Maintenance Anesthetic Agents. Chi square analyses revealed the incidence of EA was significantly greater when desflurane was used as the maintenance inhalational agent as opposed to isoflurane (* $p=0.006$). There was no significant difference in the incidence of EA between those maintained on desflurane vs sevoflurane ($p=0.4578$), or isoflurane vs sevoflurane ($p=0.3582$).

EEA and NPOBC are not associated with length of time under deep anesthesia

				t-test	Logistic regression	
	Present	n	Avg (SD) BIS<45 (min)	p-value	OR ^a (95% CI)	p-value
E/A	Yes	99	57.6 (41.8)			
	No	270	55.7 (40.7)	0.6833	1.036 (0.876 – 1.224)	0.6824
NPOBC	Yes	28	48.1 (48.6)			
	No	290	56.7(40.3)	0.29	0.994(0.984– 1.005)	0.29

^aOR: odds ratio (95% confidence interval) per 30 minute increase in length of time with BIS < 45. EA = Emergence Agitation; NPOBC = Negative Postoperative Behavioral Changes.

Table 2

Patient demographics and Summary of Results

Statistics calculated	All Patients			EA Patients		Non-EA patients		NPOBC Patients		Non-NPOBC Patients	
	N	Statistics		N	Statistics	N	Statistics	N	Statistics	N	Statistics
Mean age (SD)	370	4.2 (1.5)		99	4.0 (1.7)	270	4.3 (1.5)	28	4.0 (2.0)	290	4.3 (1.5)
% Females	370	48%		99	41%	270	50%	28	39%	290	49%
Mean m-YPAS (SD)	369	27.6 (9.5)		99	28.5 (11.0)	269	27.3 (8.9)	28	29.1 (11.7)	289	27.4 (9.1)
% Midazolam premedication	370	89%		99	91%	270	89%	28	93%	290	89%
% Distribution of maintenance anesthetic agent	des	30%,			41%,		26%,		24%,		29%,
	iso	61%		91	49%	256	65%	25	56%	267	62%
	sevo	9%			10%		9%		20%		9%
Minutes under deep hypnosis (SD)	370	56.2 (40.9)		99	57.6 (41.8)	270	55.7 (40.7)	28	48.1 (48.6)	290	56.7 (40.3)
Mean PAED score (SD)	370	7.3 (4.8)		99	13.4 (2.9)	270	5.1 (3.1)	28	8.1 (4.2)	290	7.2 (4.7)
Mean PHBQ score (SD)	318	1.9 (3.0)		83	2.3 (3.6)	234	1.8 (2.7)	28	9.3 (3.0)	290	1.2 (1.8)

No statistically significant differences were seen between patients with and without EA or NPOBC with regard to mean age, gender, mean m-YPAS score, % receiving midazolam premedication, or minutes under deep hypnosis.

EA = Emergence Agitation; NPOBC = Negative Postoperative Behavioral Changes; m-YPAS = modified Yale Preoperative Anxiety Scale; PAED = Post Anesthesia Emergence Delirium; PHBQ = Post Hospital Behavior Questionnaire

Table 3

Maintenance agent and the Occurrence EA and NPOBC

Agent	Behavior	Present	n	Avg (SD) BIS<45 (min)	t-test		Logistic regression	
					p-value	OR (95% CI)	p-value	
Iso	EA	Yes	45	52.5 (38.1)	0.94	1.000 (0.992–1.008)	0.94	
	EA	No	163	53.0 (42.2)				
Des	EA	Yes	37	56.2 (36.9)	0.20	0.993 (0.982–1.004)	0.20	
	EA	No	65	66.6 (40.4)				
Sevo	EA	Yes	9	62.3 (55.9)	0.38	1.008 (0.990–1.026)	0.38	
	EA	No	22	47.2 (37.3)				
Iso	NPOBC	Yes	14	42.0 (32.1)	0.30	0.992 (0.977–1.007)	0.23	
	NPOBC	No	166	54.0 (42.0)				
Des	NPOBC	Yes	6	49.8 (54.8)	0.40	0.990 (0.966–1.014)	0.40	
	NPOBC	No	77	64.0 (38.6)				
Sevo	NPOBC	Yes	5	38.7 (44.6)	0.45	0.989 (0.962–1.017)	0.44	
	NPOBC	No	24	55.4 (44.6)				

Subgroup analyses when stratifying by maintenance agent found no statistically significant association between length of time under deep hypnosis and the occurrence of either EA or NPOBC. OR: odds ratio (95% confidence interval); EA = Emergence Agitation; NPOBC = Negative Postoperative Behavioral Changes; Iso = isoflurane; Des = desflurane; Sevo = sevoflurane.

Table 4

Midazolam and the Occurrence of EA and NPOBC

						t-test	Logistic regression	
Midazolam	Behavior	Present	n	Avg (SD) BIS<45 (min)		p-value	OR (95% CI)	p-value
Yes	EA	Yes	90	56.8 (29.7)		0.81	1.001 (0.995–1.006)	0.81
	EA	No	239	55.5 (42.0)				
No	EA	Yes	9	66.1 (28.2)		0.41	1.011 (0.985–1.039)	0.40
	EA	No	31	56.9 (29.7)				
Yes	NPOBC	Yes	26	47.4 (48.4)		0.29	0.994 (0.984–1.005)	0.29
	NPOBC	No	257	56.6 (41.6)				
No	NPOBC	Yes	2	56.8 (71.8)		0.99	0.999 (0.954–1.048)	0.98
	NPOBC	No	33	57.2 (29.1)				

Subgroup analyses when separating patients receiving from those not receiving midazolam premedication found no statistically significant association between the length of time under deep hypnosis and the occurrence of either EA or NPOBC. OR: odds ratio (95% confidence interval); EA = Emergence Agitation; NPOBC = Negative Postoperative Behavioral Changes.