Hypnotic depth and the incidence of emergence agitation and negative postoperative behavioral changes

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Summary

Background: Emergence agitation (EA) and negative postoperative behavioral changes (NPOBC) are common in children, although 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 PACU and a greater occurrence of NPOBC in children after discharge.

Methods: We enrolled 400 children, 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. NPOBC were assessed using the Post-Hospital Behavior Questionnaire, completed by parents 3–5 days postoperatively. 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 <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: bispectral index; emergence agitation; hypnotic depth; negative postoperative behavioral changes

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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% to 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 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 otolaryngology (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 that 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 (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 that 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 ultrashort procedure but is performed using very deep levels of anesthesia. Within adults, titration of bispectral index (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. Secondary, 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 institutional review board 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 preexisting neurologic disorders (e.g., seizure history, developmental delay, psychiatric diagnosis), planned use of ketamine, and use of total intravenous anesthesia. We also excluded nonEnglish-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 premedication. 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 preoperative period through recovery in the PACU. A BIS range from 40 to 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 <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 postanesthesia emergence delirium scale (PAED) (Appendix 1) (23). EA was assessed continuously in the PACU from arrival through 10 min 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 to 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 six categories of symptoms, that children have been observed to experience postoperatively. The PHBQ was administered by the parents on postoperative days 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 seven 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 <50 or an electromyograph signal >50. This was to minimize the presence of potential artifact because of 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 (1 min) was used if the BIS was <45 at both the beginning and end of the interval, but only half the length of the interval (30 s) was summed if the BIS was <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 1.

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 2).

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 when compared to those maintained on isoflurane ($P = 0.006$). We found no significant difference in the incidence of EA between patients maintained on desflurane vs sevoflurane or isoflurane vs 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 were required when EA was present was

![Figure 1](image_url)

Enrollment data. A total of 400 children were enrolled. Of these 400 subjects, 30 were excluded due unanticipated protocol violations (e.g., use of total intravenous anesthesia), technical problems (e.g., failure of the bispectral index to record properly), or patient request. Of the remaining 370 eligible children, one had no data available for emergence agitation analysis, and 52 were lost to follow-up for the Post-Hospital Behavior Questionnaire.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient demographics and summary of results</th>
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<tbody>
<tr>
<td>Statistics calculated</td>
<td>All patients</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>370 4.2 (1.5)</td>
</tr>
<tr>
<td>% Females</td>
<td>370 48%</td>
</tr>
<tr>
<td>Mean m-YPAS (SD)</td>
<td>370 27.6 (9.5)</td>
</tr>
<tr>
<td>% Midazolam premedication</td>
<td>370 89%</td>
</tr>
<tr>
<td>% Distribution of maintenance anesthetic agent</td>
<td></td>
</tr>
<tr>
<td>Des</td>
<td>342 30%</td>
</tr>
<tr>
<td>Iso</td>
<td>61%</td>
</tr>
<tr>
<td>Sevo</td>
<td>9%</td>
</tr>
<tr>
<td>Minutes under deep hypnosis (SD)</td>
<td>370 56.2 (40.9)</td>
</tr>
<tr>
<td>Mean PAED score (SD)</td>
<td>370 7.3 (4.8)</td>
</tr>
<tr>
<td>Mean PHBQ score (SD)</td>
<td>318 1.9 (3.0)</td>
</tr>
</tbody>
</table>

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, postanesthesia emergence delirium; PHBQ, Post-Hospital Behavior Questionnaire; Iso, isoflurane; Des, desflurane; Sevo, sevoflurane.

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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 h whether or not EA was present.

Negative postoperative 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 2).

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Present</th>
<th>n</th>
<th>Avg (sd) BIS &lt;45 (min)</th>
<th>t-test P-value</th>
<th>Logistic regression OR (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA</td>
<td>Yes</td>
<td>99</td>
<td>57.6 (41.8)</td>
<td>0.6833</td>
<td>1.036 (0.876–1.224) 0.6824</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>270</td>
<td>55.7 (40.7)</td>
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<td></td>
</tr>
<tr>
<td>NPOBC</td>
<td>Yes</td>
<td>28</td>
<td>48.1 (48.6)</td>
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<td>0.994 (0.984–1.005) 0.29</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>290</td>
<td>56.7 (40.3)</td>
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<td></td>
</tr>
</tbody>
</table>

BIS, bispectral index; EA, emergence agitation; NPOBC, negative postoperative behavioral changes.

*aOR, odds ratio (95% confidence interval) per 30 min increase in length of time with BIS <45.*

Emergence agitation (EA) vs maintenance anesthetic agents. Chi-square analyses revealed that 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 ($P = 0.3582$).

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 <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 because of factors including different study populations, confounding factors such as pain, and importantly, the use of various subjective tools to assess the presence 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.
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 min, 30–40 min, 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. (11) found preschool age boys seemed to have a higher incidence of EA. 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 vs 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 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 preoperative anxiety levels and the occurrence of EA in the PACU. A confounding factor, however, may be the near universal use of midazolam premedication 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 because of 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 when compared to isoflurane. However, we found no difference in the incidence of EA with sevoflurane when 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.

Emergence agitation is defined as a self-limited phenomenon, but may still have physical, psychological, and financial impacts in the PACU. Potential harm to patients and postanesthesia care personnel may exist because of 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 per 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 because of 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 postoperative 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 no association with age, gender or type of maintenance inhalational agent used, and the incidence of NPOBC. Kain et al. (7) 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. Within our study population, we discovered no difference in the occurrence of NPOBC on follow-up 3–5 days postoperatively regardless of preoperative 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. Although 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 The Children’s Hospital 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 that 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 nonrandomly by the anesthesiologists in our study, we performed subgroup analyses stratifying by the type of maintenance agent used. We found no significant

<table>
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<th>Agent</th>
<th>Behavior</th>
<th>Present</th>
<th>n</th>
<th>Avg (min)</th>
<th>t-test P-value</th>
<th>Logistic regression OR (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iso</td>
<td>EA</td>
<td>Yes</td>
<td>45</td>
<td>52.5 (38.1)</td>
<td>0.94 1.000 (0.992–1.008) 0.94</td>
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<td>No</td>
<td>163</td>
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<td>EA</td>
<td>Yes</td>
<td>37</td>
<td>56.2 (36.9)</td>
<td>0.20 0.993 (0.982–1.004) 0.20</td>
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<tr>
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<td>No</td>
<td>65</td>
<td>66.6 (40.4)</td>
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<tr>
<td>Sevo</td>
<td>EA</td>
<td>Yes</td>
<td>9</td>
<td>62.3 (55.9)</td>
<td>0.38 1.008 (0.990–1.026) 0.38</td>
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<td>Yes</td>
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<td>0.30 0.992 (0.977–1.007) 0.23</td>
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<td>No</td>
<td>166</td>
<td>54.0 (42.0)</td>
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<td>NPOBC</td>
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<td>6</td>
<td>49.8 (54.8)</td>
<td>0.40 0.990 (0.966–1.014) 0.40</td>
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<td></td>
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<td>77</td>
<td>64.0 (38.6)</td>
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<td>Yes</td>
<td>5</td>
<td>38.7 (44.6)</td>
<td>0.45 0.989 (0.962–1.017) 0.44</td>
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<td></td>
<td>NPOBC</td>
<td>No</td>
<td>24</td>
<td>55.4 (44.6)</td>
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</table>

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. BIS, bispectral index; OR, odds ratio (95% confidence interval); EA, emergence agitation; NPOBC, negative postoperative behavioral changes; Iso, isoflurane; Des, desflurane; Sevo, sevoflurane.
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 that 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 premedication. 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% vs 6%, respectively, of those patients receiving or not receiving midazolam preoperatively \((P = 0.49)\). Subgroup analyses were performed, and no significant association was found 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.

### Acknowledgments

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References


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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

Patients were evaluated using the PAED 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 to 25 with higher scores indicating greater symptoms of emergence agitation.

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 bite 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 your 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 your 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?

The PHBQ, as developed by Vernon et al. (15) in 1966, was used to evaluate negative postoperative behavioral changes in the first 3–5 days postoperatively. 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’.