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Anesthesia induction, emergence, and postoperative behaviors in children with attention-deficit/hyperactivity disorders

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Summary

Background/Aim: Given the increasing prevalence of attention-deficit and attention-deficit hyperactivity disorders (ADHD), anesthesiologists are now presented with a greater number of children who are diagnosed with these conditions. This prospective, observational study was designed to compare anesthesia induction, emergence, and postoperative behaviors in children with and without ADHD.

Methods/Materials: The sample included 268 children, 4–17 years of age undergoing elective surgery with a confirmed diagnosis of ADHD. A cohort of children without ADHD, matched for age, gender, and procedure served as controls. Preoperative cooperation, induction, and emergence behaviors were measured using established scales. Postoperative maladaptive behaviors were measured using a modified Post-Hospital Behavioral Questionnaire that was administered via telephone 1 week after surgery.

Results: Children with ADHD were significantly less cooperative at induction of anesthesia compared with controls (20.9% vs 10.6% respectively, $P = 0.001$). Although some control children exhibited an increase in maladaptive behaviors postoperatively, these behaviors were significantly greater among children with ADHD. In particular, relative to their normal behaviors, children with ADHD had greater difficulties in concentration and decision-making; were more disobedient, impulsive, fidgety, had poor appetite; were difficult to talk to; and exhibited an increase in temper tantrums following surgery.

Conclusions: This is the first prospective study to our knowledge that has examined the perioperative and postoperative behaviors of children with ADHD compared to those without this disorder. These results are important in alerting anesthesiologists, parents, and teachers to the potential for difficulties during induction of anesthesia and postoperative behavioral problems at home and in school, respectively.

Keywords: attention-deficit hyperactivity disorders; anesthesia; behaviors

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Introduction

Attention-deficit disorder (ADD) and attention-deficit hyperactivity disorder (hereafter, referred to as ADHD) are characterized by inattention, impulsivity, and hyperactivity and affect approximately 2–20% of school-aged children and 1% of adults (1–3). Given the increasing prevalence of ADHD, it is thus likely that many children with these disorders will at some time present for anesthesia and surgery.

Potential issues related to anesthetizing children with these disorders include increased anxiety preoperatively, agitation during the induction of and emergence from anesthesia, postoperative behavioral changes, and interaction between anesthetic and ADHD drugs, e.g., methylphenidate (4). However, despite the clinical and societal importance of these potential interactions, there are no studies, to our knowledge, that have comprehensively examined the effects of anesthesia on children with these disorders. This study was designed, therefore, to examine the incidence and nature of induction, emergence, and posthospital behaviors among children presenting for anesthesia and surgery with a diagnosis of ADHD. The hypothesis to be tested was that children with ADHD would be less cooperative during induction of anesthesia compared to children without ADHD.

Methods

This study was approved by the University of Michigan's Institutional Review Board and informed consent was obtained from parents and guardians with child assent, as appropriate. The study sample included children between the ages of 4–17 who presented for an elective ambulatory surgical procedure requiring general anesthesia. Children were assigned to one of two cohorts based on the presence or absence of a diagnosis of ADHD. Cohort 1 included children with a physician- and parent-confirmed current diagnosis of ADD or ADHD and cohort 2 included children without ADHD matched for gender, age, and surgical procedure.

Following informed consent, parents were interviewed to elicit information on family demographics and, as appropriate, details of their child's ADHD diagnosis including medical management, if any. Preoperative observations and behaviors were recorded by trained research assistants who had no vested interest in the study or by anesthetists with no knowledge of the study purpose, at baseline, prior to any preoperative medications, and induction using a 3-point scale, where 1 = calm/cooperative, 2 = slightly anxious/tearful, and 3 = agitated/uncooperative/restraint needed (5). We chose to measure preoperative cooperation behaviors as a surrogate for anxiety as we were concerned that the standard measures of anxiety in children, e.g., the modified Yale Preoperative Anxiety Scale (6,7) and the Spielberger State-Trait Inventory for Children (STAIC) (8) may not be valid for the entire age range observed in our study. Preoperative anxiolytics (i.e., midazolam), anesthetic induction, and maintenance agents were administered at the discretion of the anesthesia care-provider, and standard monitoring (e.g., heart rate and rhythm, blood pressure, and oxygen saturation) was used in all cases. Emergence behavior was assessed by the research assistants or by nurses with no knowledge of the study purpose on awakening from anesthesia and at discharge from the postanesthesia care unit using a 4-point emergence agitation scale (where 0 = no agitation, 1 = mild, 2 = moderate [i.e., agitated/restless/nonpurposeful movement/difficult to console], and 3 = severe [i.e., extreme agitation/thrashing/kicking/nonpurposeful movement/incoherent/inconsolable]) (5,9). Details of the surgical procedure, duration of anesthesia and surgery, use of opioids and/or benzodiazepines, and anesthetic agent(s) used were recorded.

One week after surgery, postoperative behaviors were assessed via telephone interview of the child's parent using the Post-Hospital Behavior Questionnaire (PHBQ) (10). The PHBQ has been widely used to assess maladaptive and negative behavioral changes in children after hospital discharge and postoperatively and is considered to be the standard for this type of assessment (10,11). The PHBQ addresses several categories of anxiety including General Anxiety, Separation Anxiety, Sleep Anxiety, and Eating Disturbances. For the purposes of this study, 10 additional items were added to capture behaviors typically associated with ADHD. These items were based on content from the Revised Conners' Parent Rating Scale; a widely used screening tool for ADHD and other behavioral problems in children (12). Items added included changes in attention span/

concentration, ability to stay on task, impulsivity, fidgeting, and activity, etc. Changes in postoperative behaviors were scored using a 5-point Likert scale (−2 to +2) of 'much less than before' (relative to their normal baseline behavior), 'less than before,' 'same,' 'more than before, and 'much more than before.' Assessment of the frequency of postoperative maladaptive behaviors was calculated by transforming the data so that scores of −2, −1, or 0 = 0 (no) and 1 or 2 = 1 (yes/increase in negative behaviors). The scores for positive behaviors such as 'listens to you/others,' were reversed for analysis purposes.

Statistical analysis

Statistical analyses were performed using SPSS® statistical software (SPSS Inc. v16.0, Chicago, IL, USA). Descriptive data were analyzed using frequency distributions. Categorical outcome data, including cooperation and presence/absence of maladaptive behaviors, were analyzed using chi-square and Fisher's exact test, as appropriate. Comparison of normally distributed data such as age was analyzed using unpaired *t*-tests. Missing/incomplete PHBQ data were examined by group membership to determine whether nonrespondents differed substantively from respondents. Data are presented as *n* (%) and mean ± SD. Relative risks with 95% confidence intervals are also reported. Statistical significance was accepted at the 5% level ($P < 0.05$).

The sample size was based on a previous study that demonstrated an approximate 20% increase in behavioral management problems among children with ADHD undergoing dental procedures compared to children without ADHD (13). Accepting this difference as clinically significant, we required a sample size of 134 children per group ($\alpha = 0.05$, $\beta = 0.2$, two-sided).

Results

A total of 300 children were approached for enrollment in this study. Of these, 31 declined to participate. In addition, four potential control subjects were excluded as they did not fulfill the match criteria and one potential ADHD subject was excluded because their diagnosis had yet to be confirmed. Data are thus presented for 268 subjects (*n* = 134/group). There were no differences between the demographics of the two groups (Table 1). Eighty-two percent of the children with a diagnosis of ADHD were currently on medication. Of these, 44.9% had stopped taking their medication on the morning of surgery, 43.9% on the day or several days before surgery, and 11.2% had stopped taking their medication a week before surgery.

Table 1
Demographics

	Control (n = 134)	*ADHD* (n = 134)
Gender (M/F %)	59.7/40.3	70.9/29.1
Age, years	10.3 ± 3.5	10.5 ± 3.3
Race		
White	116 (86.6)	118 (88.1)
Black	6 (4.5)	11 (8.2)
Hispanic	2 (1.5)	2 (1.5)
Other	10 (7.4)	3 (2.2)
ASA Status (I–II/III)	94.8/5.2	94.8/5.2
Surgical Service		
Pediatric surgery	26 (19.5)	24 (17.9)
ENT	36 (26.9)	36 (26.9)
Radiology	19 (14.3)	20 (14.9)
Orthopedics	14 (10.5)	13 (9.7)
Urology	18 (13.5)	19 (14.2)
Ophthalmology	10 (7.5)	10 (7.5)
Oral Surgery	8 (6.0)	10 (7.5)
Other	3 (2.3)	2 (1.5)
Parent present at induction	34 (25.8)	35 (26.5)
Previous anesthetic	86 (64.2)	84 (62.7)

Data are expressed as *n* (%) and mean ± SD.
ASA, American Society of Anesthesiologists; ENT, ear nose and throat; ADHD, diagnosis of attention-deficit/hyperactivity disorders.

Table 2 describes the perioperative anesthetic management of children in the study. As shown, there were no differences between groups with respect to the use of a preoperative anxiolytic, induction and maintenance anesthetic agents, or the use of intra- and postoperative opioids. The relationship between the use of midazolam and the incidence of perioperative

Table 2
Perioperative anesthetic management

	Control	*ADHD*
Preoperative		
Benzodiazepines	59 (44.0)	54 (40.3)
Induction/Intraoperative		
Sevoflurane	72 (53.7)	87 (64.9)
Propofol	83 (61.9)	83 (61.9)
Isoflurane	95 (70.9)	101 (75.4)
Opioids	100 (74.6)	91 (67.9)
Postoperative		
Opioids	37 (27.6)	45 (33.6)

Data are expressed as *n* (%).
ADHD, diagnosis of attention-deficit/hyperactivity disorders.

Table 3
Relationship between the use of midazolam and perioperative behaviors in children with and without ADHD

	Preoperative 'calm/ cooperative'	*Induction 'calm/* cooperative'	*Emergence none/*mild'	*Maladaptive yes'*
ADHD				
Midazolam				
Yes	44 (81.5)	44 (81.5)	46 (88.5)	28 (57.1)†
No	75 (93.8)*	62 (77.5)	66 (82.5)	35 (47.9)
Control				
Midazolam				
Yes	50 (84.7)	53 (89.8)	53 (89.8)	16 (30.8)
No	71 (94.7)*	66 (88.0)	65 (86.7)	32 (32.3)

ADHD, history of attention-deficit/hyperactivity disorder.
*$P \leq 0.05$ vs midazolam corresponding 'yes' group.
†$P < 0.01$ vs midazolam 'yes' Control group.

behaviors between children with and without ADHD is described in Table 3.

Table 4 compares the preoperative and induction behaviors between children with and without ADHD. To determine risk ratios, we collapsed behavior categories to compare 'calm/cooperative' with 'slightly anxious/tearful' and 'uncooperative.' As shown, there were no differences in preoperative cooperation between groups (relative risk [95% confidence intervals] = 1.15 [0.58, 2.31]); however, children with ADHD were significantly more uncooperative during induction of anesthesia compared to the control group (1.97 [1.10, 3.57], $P = 0.011$). Of children with ADHD, 6.3% of children <10 years of age were uncooperative compared to 4.2% of children aged 10–17 (P = NS).

Table 5 compares the emergence and immediate postoperative behaviors between the two groups. As shown, there were no differences with respect to the

Table 4
Preoperative and induction behaviors

	Control	*ADHD*	*RR (95%* CI)
Preoperative cooperation			
Calm/cooperative	121 (90.3)	119 (88.8)	1.15 (0.58, 2.31)
Slightly anxious/ uncooperative	13 (9.7)	15 (11.2)	
Induction behavior			
Calm/cooperative	118 (89.4)	106 (79.1)	1.97 (1.10, 3.57)
Slightly anxious/ uncooperative	14 (10.6)	28 (20.9)*	

Data are expressed as *n* (%).
ADHD, diagnosis of attention-deficit/hyperactivity disorders; RR, relative risk; CI, confidence interval.
* $P = 0.011$ vs control.

Table 5
Emergence to Discharge Behaviors

	Control	*ADHD*	*RR (95%* CI)
Emergence behavior			
None/mild	118 (88.1)	112 (84.8)	1.15 (0.82, 1.76)
Moderate/severe	16 (11.9)	20 (15.2)	
Emergence to discharge behavior			
None/mild	120 (93.8)	123 (94.6)	0.93 (0.64, 1.66)
Moderate/severe	8 (6.2)	7 (5.4)	

Data are expressed as *n* (%).
ADHD, diagnosis of attention-deficit/hyperactivity disorders; RR, relative risk; CI, confidence interval.

emergence and recovery unit behaviors between the two groups (1.15 [0.82, 1.76] and 0.93 [0.64, 1.66]), respectively. However, children in both groups who exhibited moderate/severe emergence agitation had an increased incidence of maladaptive behaviors postoperatively compared to children with none/mild agitation (57.6% vs 39.5%, $P = 0.05$).

Twenty-nine of 268 (10.8%) parents (12 in the ADHD group and 17 controls, P = NS) did not complete the PHBQ or were simply lost to follow-up. There were no differences between respondents and nonrespondents with respect to their preoperative, induction, and emergence behaviors. Of those who completed the PHBQ, 51.6% of children with ADHD exhibited at least one postoperative maladaptive behavior (i.e., behaviors described as 'more/much more' compared with baseline normal) compared to 31.6% of children without ADHD ($P = 0.002$). The percentage of children with ADHD experiencing an 'improvement' in at least one behavior (i.e., behaviors described as 'less/much less' compared with normal) was 28.7% which was not significantly different from children without ADHD (18.8%, P = NS).

Table 6 compares the incidence of postoperative maladaptive behaviors between groups. These data show that, compared with control children, those with ADHD had greater increases from normal in specific maladaptive behaviors including, fidgeting, impulsivity, disobedience, difficulty concentrating, temper tantrums, difficulty communicating, and loss of appetite.

Children with ADHD who were on medication had similar preoperative induction and maladaptive behaviors compared with those children who were not. Eighty-eight percent and 77.3% of children who were on ADHD medications were cooperative

Table 6
Percentage of parents who reported their child's postoperative behaviors as 'more/much more' than normal

Behavior	*Control*	*ADHD*	*RR (95% CI)*
Overall activity	4.3	8.2	2.14 (0.48, 1.27)
Bites Nails	0.0	4.1	∞
Disinterest with toys/games	1.7	5.7	3.36 (0.71, 15.8)
Disobeys you/others	0.9	10.7*	12.4 (1.64, 92.9)
Is Forgetful	0.9	5.7	6.71 (0.84, 53.7)
Is restless/fidgety	9.4	21.3*	2.27 (1.17, 4.38)
Has trouble falling asleep	12.8	20.5	1.59 (0.89, 2.88)
Wakes upset/crying	3.4	4.1	1.20 (0.33, 4.36)
Afraid to leave your side	7.7	9.0	1.17 (0.50, 2.73)
Afraid to leave home/go to school	2.6	4.1	1.59 (0.39, 6.54)
Breaks toys/other things	0.0	0.8	∞
Is impulsive	2.6	10.7*	4.16 (1.21, 14.21)
Attention span	2.6	4.9	1.92 (0.49, 7.49)
Has a poor appetite	10.3	21.3*	2.08 (1.10, 3.92)
Difficulty deciding	2.6	10.7*	4.16 (1.21, 14.21)
Difficulty concentrating	2.6	13.1*	5.11 (1.53, 17.09)
Listens to you/others	1.7	5.7	2.88 (0.30, 27.27)
Difficult to talk too	3.4	13.1*	3.84 (1.32, 11.14)
Has temper tantrums	5.1	13.1*	2.56 (1.04, 6.31)

ADHD, history of attention-deficit/hyperactivity disorder; RR, relative risk; CI, confidence interval.
*$P < 0.05$ vs control.

preoperatively and on induction, respectively, compared with 91.7% and 87.5% who were not currently taking medication (P = NS). Similarly, 50% of children on medication exhibited at least one postoperative maladaptive behavior compared with 59.1% who were not on medication. However, children with ADHD who were taking medication for their disorder had greater difficulty sleeping (25.0%) after surgery compared to those who were not currently on medication (10.9%; $P = 0.004$).

Discussion

To our knowledge, this is the first prospective study examining perioperative behaviors in children with ADHD. Results suggest that children with ADHD are more uncooperative on induction of anesthesia and are more likely to exhibit exaggerated postoperative maladaptive behavioral changes compared to children without these disorders. The former finding is important with respect to the clinical management of these patients and the latter may be important in terms of alerting parents and teachers to the possibility of negative postoperative behavioral issues seen at home and in school, respectively.

Previous studies have shown that preoperative anxiety is a risk factor for poor behavioral compliance during induction of anesthesia and postoperative maladaptive behaviors in young children (11,14). Although we did not measure anxiety *per se*, we found that children with ADHD were more likely to be uncooperative on induction of anesthesia. In a study by Blomqvist *et al.* (15), children with ADHD undergoing dental procedures exhibited similar anxiety levels to control children but had a higher prevalence of behavior management problems. In another study by the same authors, children with ADHD undergoing dental procedures were shown to have significantly lower cortisol levels than children without ADHD yet were harder to manage clinically (16). This led the authors to conclude that behavioral expressions of anxiety in children with ADHD may be different from others. Indeed, this is supported by a study which showed that children with ADHD respond differently to stress and have impaired coping skills compared with children without ADHD (17).

Several studies have shown that children without ADHD may demonstrate a number of maladaptive behaviors including sleep disturbances, separation anxiety, disobedience, and temper tantrums for several weeks following general anesthesia (18–20). In one study, 47% of children were noted to exhibit problematical behavior following day-case surgery (18). Although these behaviors appear to be independent of the anesthetic used (21), Kain *et al.* identified several predictors of postoperative maladaptive behaviors including preoperative anxiety in the holding room, overall anxiety, and the presence of emergence delirium (11,19). In concert with these findings, we also showed an association between emergence agitation and postoperative maladaptive behaviors in both groups. The reasons for this are unclear, but may be related to the child's underlying temperament and, in particular, the way in which certain children react and adapt to external stimuli and stress (22,23). Indeed, in one study, Voepel-Lewis *et al.* (5) showed that children with low adaptability were more likely to experience emergence agitation and, in another, Kain *et al.* (23) showed that children who were very impulsive were more likely to exhibit negative behaviors postoperatively. Unlike Kain's *et al.* study, we did not find an association between preoperative and postoperative

behaviors; however, this may be because of the fact that we were measuring cooperation rather than anxiety *per se* and this may explain the difference in findings.

Both children with and without ADHD reported increased difficulty sleeping following surgery (20.5% vs 12.8%, respectively, P = NS). This observation reinforces the findings of Caldwell-Andrews *et al.* (24) who showed that healthy children exhibit increased postoperative sleep disturbances following surgery. These authors also noted that sleep problems were associated with child aggressive behaviors and parental anxiety. In a study of children with ADHD, Sung *et al.* (25) demonstrated an increased prevalence of sleep problems sufficient to severely impact the child, family, and school dynamics. Indeed, there is also some suggestion that certain types of ADHD are associated with obstructive sleep apnea and interrupted sleep patterns (26). While we observed an overall trend toward an increased frequency of sleep disturbances among all children with a history of ADHD, those who were currently taking medication had an even greater exacerbation of sleep problems compared to those who were not on medication. Although the reason for this is unclear, it may be due, in part, to the stimulant effects of the medications used to treat ADHD. Importantly, as the PHBQ only measures change from baseline in sleep disturbances, not merely their presence or absence, it remains unclear whether children with ADHD in this study had a greater prevalence of sleep disturbances at baseline. In any case, the observation that sleep disturbances are exacerbated following surgery in all children is important as a means to alert parents and teachers of the potential for increased somnolence at home and in the classroom.

Several potential interactions between anesthetic and ADHD drugs have been postulated; however, there are very little data to suggest that these are clinically important (4). One potential consequence of anesthetic–ADHD drug interactions may be inadequate sedation. In one case report, Ririe *et al.* (27) showed that the drug methylphenidate (Ritalin) reduced the effectiveness of midazolam in a 6-year-old child requiring conscious sedation for an echocardiogram. Despite additional doses of midazolam and ketamine, sedation remained inadequate. The authors postulated that the stimulant effect of the methylphenidate may have antagonized the sedative effect of the midazolam. In two other studies in adults, methylphenidate was shown to reduce sedation for up to 30 min following surgery (28) and increase anesthetic induction requirements, respectively (29). In our study, there were no differences in cooperation between children who received midazolam in the presence or absence of ADHD medications. However, children with ADHD who received midazolam were more likely to exhibit postoperative maladaptive behaviors compared with children without ADHD receiving the same anxiolytic.

A few points regarding the limitations of the study deserve mention. First, this is a nonrandomized, observational study and, as such, there is some potential for selection bias. All children with a confirmed diagnosis of ADHD were included in the study and the controls matched with respect to age, gender, and surgical procedure. While we were unable to standardize the anesthetic regimens, both groups appeared to be fairly similar other than the diagnosis of ADHD. Second, although it was not possible to blind everybody to the ADHD status of the subject, we should note that most of the outcome data were recorded by individuals who were unaware that we were specifically studying children with ADHD. Third, we were unable to document when the children with ADHD resumed their medications following surgery. Although there are no formal guidelines for the resumption of ADHD medications following surgery at our institution, general recommendations follow those of other medications i.e., that they be resumed as soon as the child is able to take solid food. Thus, we have no reason to believe that resumption of medications was delayed. Fourth, it may be that parents of children with ADHD are more sensitive to their child's behaviors and thus may be more likely to over-report behaviors compared with parents of children without ADHD. While this may be true, the fact that the PHBQ reports changes in behaviors relative to normal should counteract any effect of over-reporting as both pre- and postoperative behaviors would be equally reported. Lastly, we recognize that as the sample size was based on expected differences in induction behaviors between groups, the sample may not have been sufficiently powered to detect all other univariate and multivariate comparisons.

Although there have been a few studies that have examined the behaviors of children with ADHD undergoing dental procedures, we believe that this is the first study to examine perioperative behaviors in children with ADHD. The results confirmed our hypothesis that children with a history of ADHD are more likely to be uncooperative during induction of anesthesia and have a greater frequency of postoperative maladaptive behaviors compared with children without these disorders. These results, therefore, are important in alerting anesthesiologists, parents, and teachers to the potential for difficulties during induction of anesthesia and postoperative behavioral problems at home and in school, respectively.

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