

END-TIDAL CARBON DIOXIDE DURING PEDIATRIC PSG

End-Tidal Carbon Dioxide Measurement during Pediatric Polysomnography: Signal Quality, Association with Apnea Severity, and Prediction of Neurobehavioral Outcomes

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Study Objectives: To identify the role of end-tidal carbon dioxide (EtCO₂) monitoring during polysomnography in evaluation of children with obstructive sleep apnea syndrome (OSAS), including the correlation of EtCO₂ with other measures of OSAS and prediction of changes in cognition and behavior after adenotonsillectomy.

Design: Analysis of screening and endpoint data from the Childhood Adenotonsillectomy Trial, a randomized, controlled, multicenter study comparing early adenotonsillectomy (eAT) to watchful waiting/supportive care (WWSC) in children with OSAS.

Setting: Multisite clinical referral settings.

Participants: Children, ages 5.0 to 9.9 y with suspected sleep apnea.

Interventions: eAT or WWSC.

Measurements and Results: Quality EtCO₂ waveforms were present for ≥ 75% of total sleep time (TST) in 876 of 960 (91.3%) screening polysomnograms. Among the 322 children who were randomized, 55 (17%) met pediatric criteria for hypoventilation. The mean TST with EtCO₂ > 50 mmHg was modestly correlated with apnea-hypopnea index (AHI) ($r = 0.33$; $P < 0.0001$) and with oxygen saturation ≤ 92% ($r = 0.26$; $P < 0.0001$). After adjusting for AHI, obesity, and other factors, EtCO₂ > 50 mmHg was higher in African American children than others. The TST with EtCO₂ > 50 mmHg decreased significantly more after eAT than WWSC. In adjusted analyses, baseline TST with EtCO₂ > 50 mmHg did not predict postoperative changes in cognitive and behavioral measurements.

Conclusions: Among children with suspected obstructive sleep apnea syndrome, overnight end-tidal carbon dioxide (EtCO₂) levels are weakly to modestly correlated with other polysomnographic indices and therefore provide independent information on hypoventilation. EtCO₂ levels improve with adenotonsillectomy but are not as responsive as AHI and do not provide independent prediction of cognitive or behavioral response to surgery.

Clinical Trial Registration: Childhood Adenotonsillectomy Study for Children with OSAS (CHAT). ClinicalTrials.gov Identifier #NCT00560859.

Keywords: capnography, CO₂, end-tidal, hypercapnia, hypoventilation, pediatric, polysomnogram, sleep apnea

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INTRODUCTION

The American Academy of Sleep Medicine (AASM) Manual for Scoring of Sleep and Associated Events recommends monitoring for hypoventilation on diagnostic polysomnograms (PSGs) in children.¹ Nasal exhaled end-tidal carbon dioxide (EtCO₂) by capnography is the most commonly used surrogate for CO₂ measurement in children. This signal is relatively easy to measure from the same cannula-type sensor that measures the nasal pressure signal. Furthermore, a PSG pattern of obstructive hypoventilation, defined as at least 25% of total sleep time (TST) with hypercapnia (partial pressure of

carbon dioxide [PaCO₂] > 50 mmHg) in association with other clinical sleep disordered breathing findings is a diagnostic criteria for pediatric obstructive sleep apnea syndrome (OSAS).² However, the recommendation for the scoring of hypoventilation is based on consensus with limited evidence of the added value of EtCO₂ monitoring in the diagnosis of OSAS. Collection of capnographic data increases equipment costs and staff time, so any additional justification for the measurement is important.

Smaller studies have previously described EtCO₂ correlations with polysomnographic variables and demographic variables such as obesity and age.^{3–8} However, the added value of the EtCO₂ signal in identification of OSAS and its severity, beyond measurement of apneas, hypopneas, oxygen saturation, arousals, and sleep stage distribution, has not been established with a large pediatric sample; neither has the important question of whether hypercapnia identifies subgroups who respond differently to OSAS treatment.

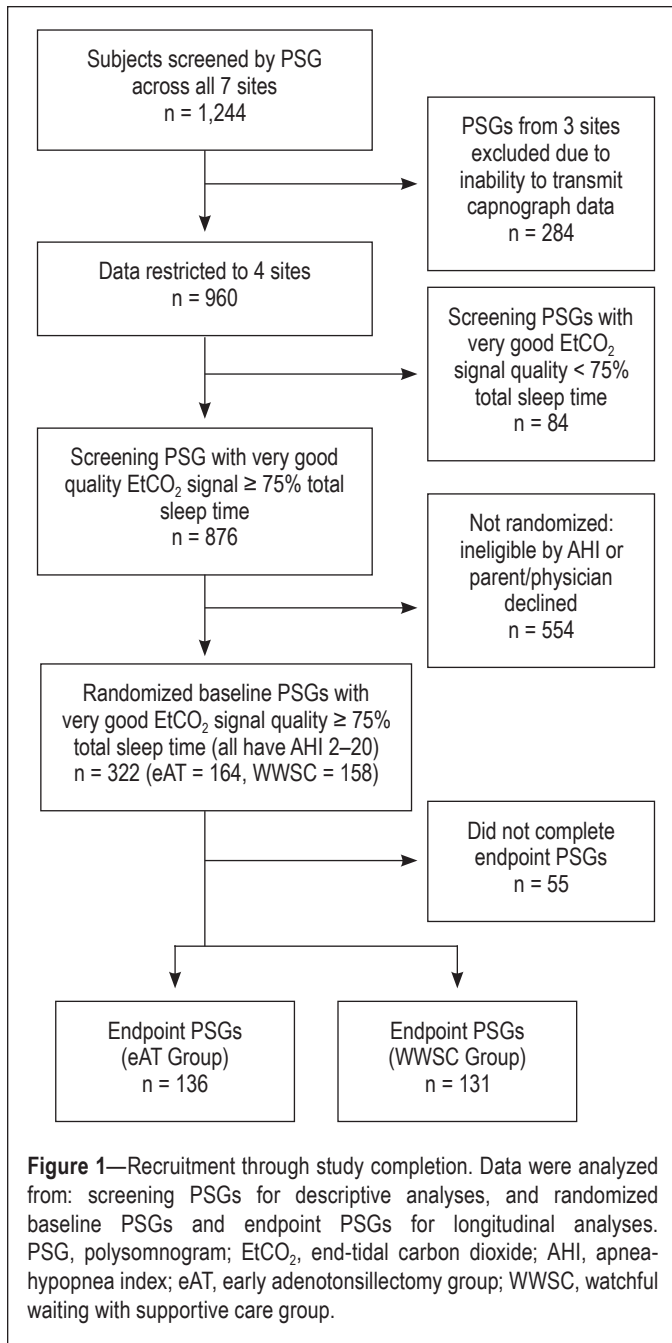
In this report, we analyze rigorously collected, multicenter capnography data, with an explicit interest in quantifying

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EtCO₂ signal quality in children likely to have nasal obstruction from adenoid hypertrophy. We tested the added value of capnography data in characterizing OSAS disease severity by quantifying its correlation with the apnea-hypopnea index (AHI) and other polysomnographic indices. Last, we determined whether baseline level of hypercapnia is associated with lower measures of cognition and behavior at baseline, shows responsiveness to adenotonsillectomy, or predicts greater improvements in health outcomes following early adenotonsillectomy (eAT) compared with watchful waiting with supportive care (WWSC). We hypothesized that: (1) increased hypercapnia would correlate with greater severity of OSAS as measured by AHI and other polysomnographic indices; (2) hypercapnia would improve following adenotonsillectomy; and (3) the presence of hypercapnia would be associated with worse cognitive and behavioral outcomes.

METHODS

The study was approved by the Institutional Review Board of each participating institution. Informed consent was obtained from caregivers, and assent from children at least 7 y of age.

Data were examined for descriptive analyses and for longitudinal analyses at multiple time points from the Childhood Adenotonsillectomy Trial (CHAT): 960 screening PSGs for cross-sectional analyses; and 366 baseline PSGs (randomized participants) and 325 follow-up PSGs (endpoint) for longitudinal analyses (see Figure 1).

The design of the CHAT study has been previously described in detail⁹ and the primary cognitive and behavioral outcomes have been published.¹⁰ In brief, the CHAT study screened children ages 5.0–9.9 y with parental report of snoring. Exclusion criteria included recurrent tonsillitis, cardiovascular comorbidities, medication use for attention deficit/hyperactivity disorder or psychiatric disorders, body mass index (BMI) z-score ≥ 3, developmental delays requiring school accommodations, and known genetic, craniofacial, or neurological disorders likely to affect the airway, cognition, or behavior.

Seven sites recruited children from sleep centers, otolaryngology clinics, general pediatrics clinics, and the general community; three sites (n = 284 of 1,244) were excluded in the current analyses because of inability to transmit the capnography data from local polysomnographic systems to a central reading center. Children who snored and were adenotonsillectomy candidates with PSGs showing an obstructive apnea index (OAI) ≥ 1/h or AHI ≥ 2/h were eligible for randomization. Children with severe OSAS, defined as OAI > 20, AHI > 30, or percentage of sleep time with an oxygen saturation < 90% for > 2% TST were ineligible for randomization.

Children underwent standardized evaluations of anthropometric characteristics, cognitive and behavioral functions, and other measures at baseline and 6 mo after the intervention period. The following neurocognitive and behavioral assessments were completed: Developmental Neuropsychological Assessment (NEPSY)¹¹ Attention/Executive Function using subtests Tower, Auditory, Visual Attention, Inhibition, and Word Generation to create the Core Domain score, the Conners Rating Scale Revised: long version using the Global Index Total T-score,¹² and the Behavior Rating Inventory of Executive Function (BRIEF) using the Global Executive Composite score.¹³

Description of Signal Collection

Each child underwent a standardized screening PSG at baseline and endpoint, which were centrally scored by registered PSG technologists. All PSGs were performed in an accredited academic sleep laboratory.

Sites collected EtCO₂ data on either the Novamatrix Capnograph (Respironics, Wallingford, CT) or the BCI Capnocheck (Smiths Medical, Waukesha, WI). BCI capnographs were used for EtCO₂ collection on 43 PSGs in Cincinnati and 60 PSGs in Cleveland. Novamatrix capnographs were used for EtCO₂ collection in the other 857 PSGs. Because a small systematic difference in values from the two capnographs was observed in a substudy of 19 PSGs where both devices were used simultaneously (e.g., mean peak EtCO₂ 52.6 ± 4.1 SD versus 51.8 ± 4.3 mmHg for BCI versus Novamatrix), the values from the BCI capnographs were adjusted using calibration equations as

shown in the Appendix. No participants had blood gas measurements to validate EtCO₂ values.

PSGs were performed, and scored in a manner consistent with recommendations of the AASM.¹⁴ The number of obstructive apneas and hypopneas per hour of sleep were calculated and reported as the AHI. Hypopneas were scored if a $\geq 50\%$ reduction in airflow was accompanied by an arousal or $\geq 3\%$ oxygen desaturation.¹⁴ For analyses, hypoventilation was defined as $> 25\%$ TST with EtCO₂ > 50 mmHg^{1,14} and hypercapnia was quantified as the percentage of sleep time > 50 mmHg. Wake EtCO₂ values were measured on the PSG, at the time of lights out and prior to sleep onset. An endpoint PSG was performed 7 mo following randomization.

Evaluation of Signal Quality

Data quality was assessed by a technologist using a five-point scale indicating percentage of sleep time when the EtCO₂ signal was available, with excellent waveform and ideal plateau signal, and free from artifact. Categories were designated by signal quality present for $> 95\%$ TST (excellent); 75–94% TST (very good); 50–74% TST (fair); 25–49% TST (poor); or $< 25\%$ TST (very poor).

Statistical Approach

Continuous variables are presented as means and standard deviations (SD) and categorical variables as percentages. Spearman correlations were used to assess associations between EtCO₂ variables and PSG variables, and between sleep measures and cognitive and behavior measures. Strength of correlations were categorized as strong (> 0.5), moderate (0.3–0.5), and weak (< 0.3).¹⁵ A kappa coefficient was used to describe agreement of classifications using EtCO₂ and AHI variables. As 13% of screening PSGs met criteria for hypoventilation, we compared this group to the top 13% of PSGs with highest AHI values (AHI > 8.7). Two-sample *t*-tests were used to test whether the distributions of a continuous variable were similar between two independent groups. Paired *t*-tests were used to assess whether the distributions of a continuous variable were similar at screening and at endpoint. Chi-squared or Fisher exact tests (when the cell counts were small) were used to compare categorical variables. Multiple linear regression models were performed to assess association of EtCO₂ with cognitive and behavioral measures while controlling for age, sex, and race. Analyses were restricted to only PSGs with “very good” quality EtCO₂ signal for $\geq 75\%$ of TST ($n = 876$; 91%). *P* values of less than 0.05 were considered to indicate statistical significance without multiple comparison adjustment. All statistical analyses were performed using SAS, version 9.3 (SAS Institute, Inc., Cary, NC).

RESULTS

Descriptive Analyses of Screening PSGs

EtCO₂ Sensor Device Comparison and Signal Quality

Screening data were available for 960 subjects from four clinical sites. In general, the acquisition of “very good” quality signal (i.e., $\geq 75\%$ TST) across the four sites was comparable, with more site-to-site variability in the proportion of signals with “excellent” signal quality (i.e., $\geq 95\%$ of TST).

Table 1—Baseline demographics, EtCO₂ values and PSG variables in children with EtCO₂ signal quality interpretable $\geq 75\%$ total sleep time ($n = 876$).

Demographics	
Age, y	7.1 \pm 1.4, (5.9, 8.3)
Male	412 (47.1%)
African American	458 (52.8%)
Obese	262 (30.8%)
EtCO ₂ variables, mmHg	
EtCO ₂ peak, mmHg	54.1 \pm 4.0, 54.0 (51.5, 56.3)
Baseline EtCO ₂ , awake, mmHg	41.7 \pm 3.0, 41.8 (39.8, 43.7)
Baseline EtCO ₂ , asleep, mmHg	44.7 \pm 3.3, 45.0 (42.7, 47.0)
% TST EtCO ₂ > 50 mmHg	9.1 \pm 18.1, 0.8 (0.2, 6.8)
Hypoventilation (EtCO ₂ > 50 mmHg for $> 25\%$ TST)	116 (13.2%)
PSG variables	
AHI (N/h)	4.5 \pm 8.5, 1.5 (0.5, 4.8)
Arousal index (N/h)	7.8 \pm 3.8, 7.1 (5.6, 9.1)
SaO ₂ $\leq 92\%$ (%TST)	0.6 \pm 3.0, 0 (0, 0.1)
Sleep efficiency (%)	85.8 \pm 8.8, 88.2 (81.6, 92.0)

Statistics shown for categorical variables are *n* (%) from the population with available data as continuous variables are mean \pm SD, median (Q1, Q3). AHI, apnea-hypopnea index; EtCO₂, end-tidal carbon dioxide; SaO₂, saturation of oxygen; SD, standard deviation; TST, total sleep time.

Interpretable EtCO₂ waveforms, graded as “very good,” were present for $> 90\%$ of children ($n = 876$) using a standardized protocol performed by certified technicians. Of the 325 children who were randomized and completed the endpoint PSG, 296 (91%) had EtCO₂ signals graded as “very good”. Reasons listed by technicians for signal loss included mouth breathing, moisture in the nasal cannula, incorrect position of cannula in nares, or equipment and technical difficulties. The signal quality for baseline PSGs of randomized subjects was similar between the eAT arm and the WWSC arm ($P = 0.44$).

EtCO₂ Correlations with Demographic Variables

Table 1 summarizes the patient demographics and PSG variables in the screening sample with “very good” or better signal quality: 412 participants (47.1%) were boys, 458 (52.8%) were African American (AA), and 262 (30.8%) were obese. African American children had a higher percentage of TST with EtCO₂ > 50 mmHg than non-AA children ($P = 0.0004$). Compared to non-AA children, AA children also had higher values for baseline wake EtCO₂, baseline sleep EtCO₂, maximum (peak) EtCO₂, mean rapid eye movement EtCO₂, and mean non-rapid eye movement EtCO₂. These associations persisted after adjustment for age, sex, obesity and AHI (all *P* values < 0.03). EtCO₂ variables were not associated with age or sex.

Relationships between EtCO₂ Values and PSG Variables

Increasing EtCO₂ values were associated with AHI severity levels (Figures 2 and 3). Percentage of TST with EtCO₂ > 50 mmHg was modestly correlated with AHI ($r = 0.33$; $P < 0.0001$) and with percentage of TST spent with oxygen

saturation $\leq 92\%$ ($r = 0.26$; $P < 0.0001$); and weakly correlated with sleep efficiency ($r = 0.08$; $P = 0.017$). Similarly, peak EtCO_2 values were modestly correlated with obstructive AHI ($r = 0.31$; $P < 0.0001$) and percentage of TST with oxygen saturation $\leq 92\%$ ($r = 0.29$; $P < 0.0001$), and weakly correlated with sleep efficiency ($r = 0.11$; $P = 0.0012$). Arousal index did not correlate with either percent of TST with $\text{EtCO}_2 > 50$ mmHg or peak EtCO_2 ($P = 0.085$ and 0.64); neither did average saturation of oxygen (SaO_2 , $P = 0.16$ and $P = 0.36$).

Among the 876 screening PSGs, 116 (13.2%) showed $\text{EtCO}_2 > 50$ mmHg for $> 25\%$ TST, meeting the criteria for hypoventilation. The agreement between percentage of TST with $\text{EtCO}_2 > 50$ mmHg and AHI severity was compared using the top 13th percentiles of these two variables. Of 116 subjects with hypoventilation, 40 had AHI values in the top 13th percentile, showing only a modest agreement ($\text{kappa} = 0.24$, 95% confidence interval [CI]: 0.16–0.33).

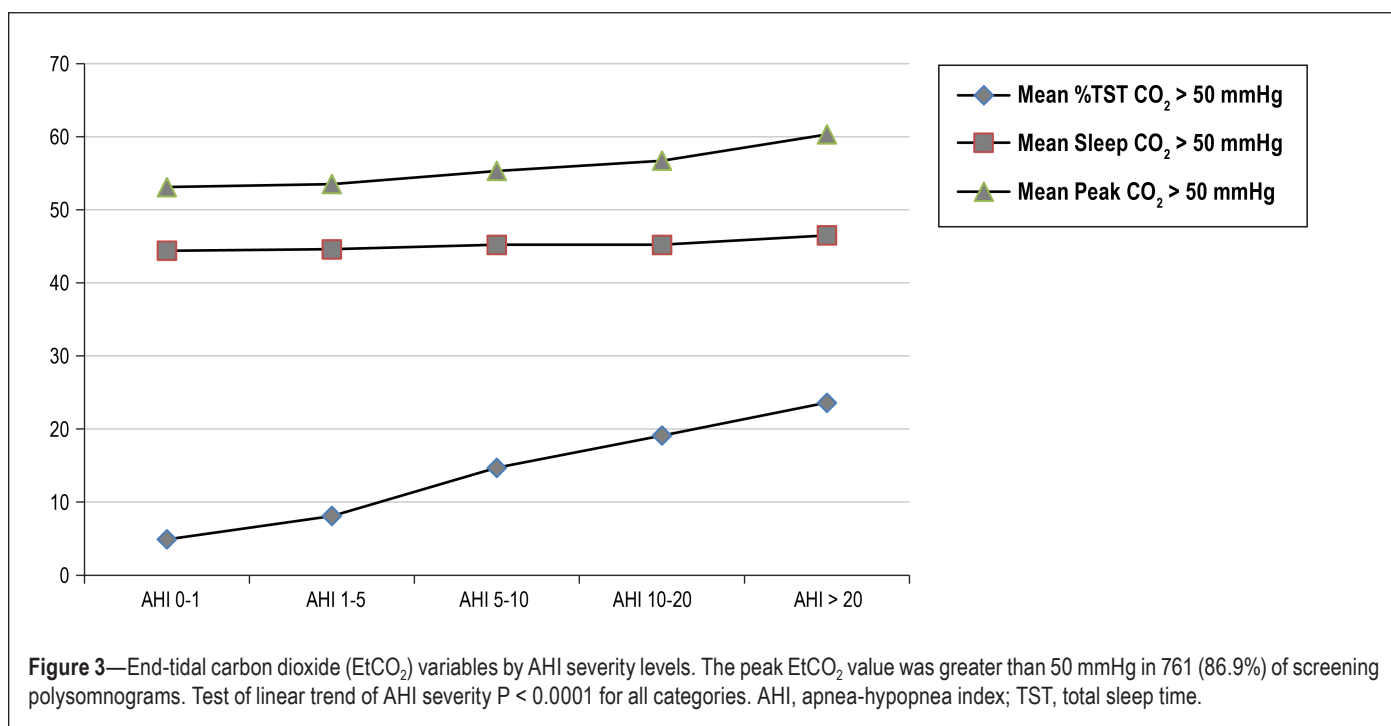
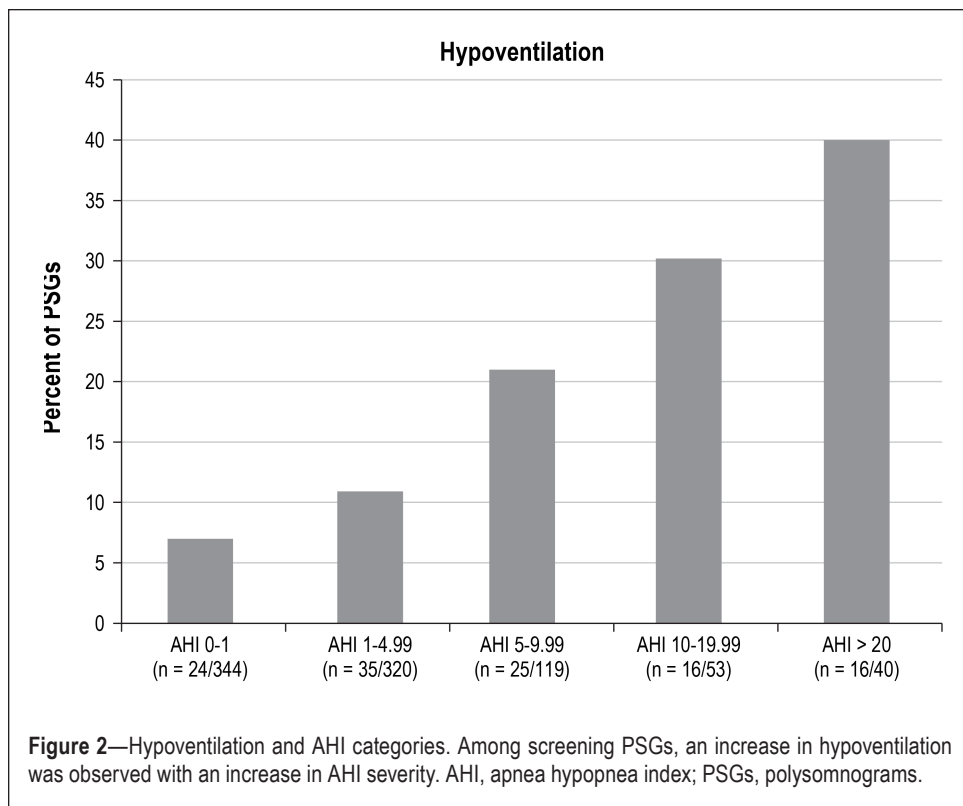
EtCO₂ Levels Compared during Wake and Sleep

Among the 876 screening PSGs with at least very good signal quality, mean sleep EtCO_2 values were higher than wake values by an average of $3.0 \text{ mmHg} \pm 1.8 \text{ mmHg}$ ($P < 0.0001$); with a maximum difference of 9 mmHg.

Longitudinal Analyses of Baseline and Endpoint PSGs of Randomized Participants

Change in EtCO₂ Values at Endpoint: eAT Compared with WWSC

The %TST $\text{EtCO}_2 > 50$ mmHg showed significantly more improvement after 6 mo in the eAT group compared to the WWSC group ($P = 0.010$, Cohen d effect size of 0.32). In contrast, the AHI improvement in the eAT group relative to the WWSC group was approximately twice as high as the improvement in EtCO_2 between



groups ($P < 0.0001$, Cohen d effect size of -0.61). See Figure 4.

Change in Hypoventilation on PSGs

Among the 876 screening PSGs evaluated, 116 (13%) met the criteria for hypoventilation and OSAS. Among the 322 children randomized, 55 (17%) met criteria for hypoventilation, 40 of whom had baseline and endpoint PSGs (25 from the eAT group; 15 from the WWSC group). Of these 40 children, 7 of 25 children in the eAT group had persistent hypoventilation and 13 of 25 had persistent AHI > 1 at follow-up. In the WWSC group, 6 of 15 children had persistent hypoventilation and 11 of 15 had persistent AHI > 1 at follow-up. Of the 25 children

in the eAT group who met criteria for baseline hypoventilation, the mean sleep EtCO₂ was 49.5 mmHg on the baseline PSG and improved to 46.6 mmHg on the endpoint PSG, with a change of -2.8 mmHg (95% CI $[-3.9, -1.7]$, $P < 0.0001$). A similar change was observed in the 15 children in the WWSC group who met criteria for hypoventilation, with a mean sleep EtCO₂ of 49.4 mmHg on the baseline PSG that improved to 46.7 mmHg on the endpoint PSG, with a change of -2.7 mmHg (95% CI $[-4.5, -1.0]$, $P = 0.05$). See Figure 5.

In the subset of children who underwent adenotonsillectomy and had a subsequent AHI $< 1/h$ ($n = 84$), the %TST EtCO₂ > 50 mmHg decreased significantly from $11.7\% \pm 20.9\%$ at baseline to $6.7\% \pm 12.8\%$ at follow-up ($P = 0.03$). Of these 84 children, 12 met criteria for hypoventilation on the baseline PSG whereas 3 children still met criteria for hypoventilation on the endpoint PSG. Mean wake EtCO₂ values and mean sleep EtCO₂ values were similar for baseline and endpoint PSGs ($P = 0.91$ and $P = 0.69$).

There were 227 randomized children who did not meet criteria for hypoventilation at baseline and had follow-up PSGs. In the eAT group, hypoventilation developed in 5 of the children (4.5%) and 39 (35%) had an AHI > 1 at endpoint. In the WWSC group, hypoventilation developed in 14 (12%) and 84 (72%) had an AHI > 1 at endpoint.

Change in Wake EtCO₂ Levels

Among the baseline PSGs, 15.7% (42 of 267) showed mean wake EtCO₂ values > 45 mmHg (eAT = 26 and WWSC = 16).

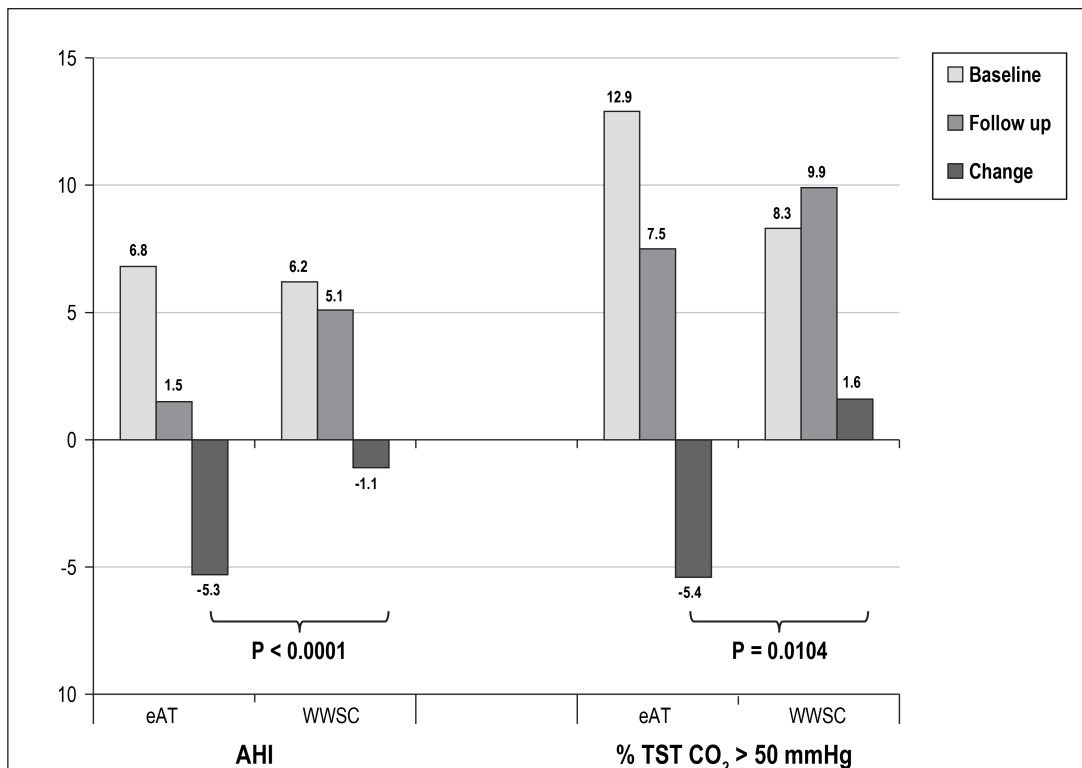


Figure 4—Comparison of AHI and percentage TST end-tidal carbon dioxide > 50 mmHg before and after adenotonsillectomy. A total of 267 children had baseline and endpoint polysomnogram data available ($n = 136$ eAT group; $n = 131$ WWSC group). AHI, apnea hypopnea index; eAT, early adenotonsillectomy; TST, total sleep time; WWSC, watchful waiting with supportive care.

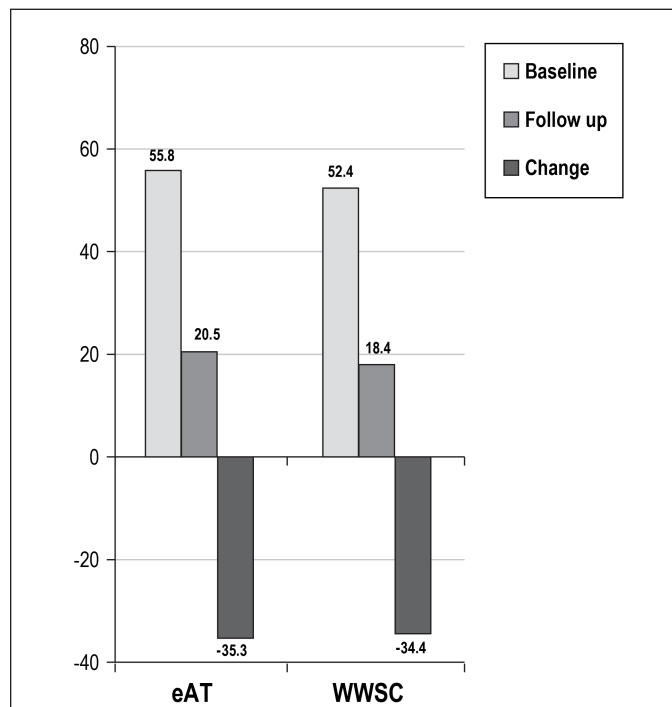


Figure 5—Change in hypercapnia in children with hypoventilation. Change in %total sleep time end-tidal carbon dioxide > 50 mmHg in randomized subjects who had hypoventilation on the baseline polysomnogram with follow-up data on endpoint polysomnogram ($n = 25$ eAT group; $n = 15$ WWSC group). eAT, early adenotonsillectomy; WWSC, watchful waiting with supportive care.

Table 2—Polysomnographic variables and changes in cognitive measures.

	NEPSY (Attention/Executive Function), n = 260		Conners Rating Scale, n = 256		BRIEF, n = 256	
	Spearman	P value	Spearman	P value	Spearman	P value
EtCO ₂						
% TST EtCO ₂ > 50 mmHg	-0.012	0.85	-0.090	0.15	-0.059	0.35
Additional PSG variables						
AHI (N/h)	0.001	0.99	-0.065	0.30	-0.005	0.93
Arousal index (N/h)	0.010	0.87	-0.061	0.33	-0.035	0.58
SaO ₂ ≤ 92% (%TST)	0.018	0.77	0.037	0.56	0.030	0.63
Sleep efficiency (%)	0.036	0.56	0.080	0.20	0.042	0.50

Statistics shown are Spearman correlation coefficient and P value. NEPSY, Conners Rating Scale, and BRIEF scores showed a weak, nonsignificant correlation to polysomnogram measures. AHI, apnea-hypopnea index; BRIEF, Behavior Rating Inventory of Executive Function; Global Executive Composite Score Conners Rating Scale, Conners Rating Scale, Revised: long version; Global Index Total T-Score; EtCO₂, end-tidal carbon dioxide; NEPSY, Developmental Neuropsychological Assessment Core Domain Score, Attention/Executive Function Scaled Score; PSG, polysomnogram; SaO₂, saturation of oxygen; TST, total sleep time.

Among endpoint PSGs, 14.6% (39 of 267) PSGs showed average wake EtCO₂ > 45 mmHg (eAT = 19 and WWSC = 20). Only two screening baseline PSGs showed an average wake EtCO₂ > 50 mmHg, one each, in the eAT and WWSC groups. Only one endpoint PSG was identified with an average wake EtCO₂ > 50 mmHg in the WWSC group.

Hypercapnia and Cognitive or Behavioral Outcomes

Baseline cognitive and behavioral parameters did not differ between children with hypercapnia and those without hypercapnia at baseline ($P > 0.6$). The baseline percentage of TST with EtCO₂ > 50 mmHg did not correlate with changes on the cognitive and behavioral assessments at follow-up (see Table 2, $r = -0.09$ to -0.012 , all $P > 0.15$). When controlling for age, sex, race, and the treatment assignment, the baseline percentage of TST with EtCO₂ > 50 mmHg did not predict changes on the cognitive and behavioral assessments at follow-up ($P > 0.3$).

DISCUSSION

This analysis of rigorously collected data from a large, randomized controlled trial of adenotonsillectomy for the treatment of pediatric OSAS identified several novel findings regarding EtCO₂ levels in children undergoing polysomnography: (1) high-quality EtCO₂ waveforms can be obtained from multiple sites in children with suspected OSAS using a standardized protocol performed by trained technicians; (2) approximately 13% of adenotonsillectomy candidates meet criteria for hypoventilation, including 5% with AHI levels < 1; (3) increasing EtCO₂ values are associated with increasing AHI levels as well as levels of hypoxemia, although the correlations are modest; (4) increased EtCO₂ levels and hypoventilation are more common in African American children than other children, even after adjusting for AHI and obesity; (5) EtCO₂ levels improve significantly more with eAT than WWSC, but the effect size (or “responsiveness to surgery”) is less than for AHI change; (6) approximately 30% of children with hypoventilation at baseline have persistence of this after surgery; (7) neither baseline hypercapnia or change in EtCO₂ levels predict baseline or change in cognitive and behavioral parameters. In aggregate, these findings indicate that

collection of high-quality EtCO₂ data in children with OSAS is feasible in multicenter studies; that there is unique information in EtCO₂ signals, including identification of children with hypoventilation (and groups at risk for hypoventilation such as African Americans); but that there is no evidence supporting a role of EtCO₂ monitoring for predicting behavioral or cognitive outcomes.

Although capnography data collection may be difficult, particularly in younger children with limited ability to cooperate with nasal sensors, our study shows that the capnography waveform was interpretable for more than 90% of children, even in the presence of adenotonsillar hypertrophy. Pediatric-focused technicians trained to perform basic troubleshooting protocols for this sensor was an important strategy for quality data collection. Sleep laboratory supervisors and technicians participated in monthly conference calls with the centralized scoring center to identify areas of improvement in data collection, which may have contributed to data quality. Despite these standardized protocols and training for all technicians in the CHAT study, a small amount of site-to-site variability in signal quality was observed. This may be due to different technical expertise in managing these sensors and highlights the importance of experienced pediatric technicians when high-quality data are needed. Nevertheless, the overall proportion of PSGs with very good EtCO₂ signal was high.

We found that 13.2% of the CHAT participants met criteria for hypoventilation. This prevalence is higher than the reported prevalence of 2.2% children with hypercapnia in normative pediatric samples.^{3,6} This higher prevalence in our sample is likely related to a PSG-based diagnosis of OSA in all participants who were also clinically symptomatic.

As we had hypothesized, increased OSAS severity as measured by the AHI and time at low oxygen saturation levels, correlated with increased TST with EtCO₂ > 50 mmHg, providing evidence for convergent validity for these measures, though modestly. In particular, classification of normal or severe OSAS using various threshold values for the AHI, level of overnight hypoxemia, and level of EtCO₂ identified overlapping, but not synonymous subsets of children. Our results

do not indicate whether the children uniquely identified with high EtCO₂ levels are a subset that require alternative management or have a different prognosis. However, the finding that African American children were more likely to have hypoventilation in analyses adjusted for AHI and obesity suggests that EtCO₂ monitoring may be useful for identifying children at increased risk for OSAS and its comorbidities. We also did not observe measures of EtCO₂ to be more responsive to surgery than the AHI. In our study, EtCO₂ measurements did not provide predictive information regarding baseline or postoperative cognition or behavior outcomes. However, a recent study showed that increased EtCO₂ values were associated with increased risk of perioperative respiratory complications after adenotonsillectomy.¹⁶

An interesting observation was the finding that almost 5% of our sample with an AHI < 1/h on PSG met the EtCO₂ criteria for hypoventilation. We assessed for hypoventilation in children with AHI < 1/h, as a current definition for OSAS in the International Classification of Sleep Disorders, Third Edition² includes PSG with AHI > 1. A previous study of healthy, nonsnoring children reported that 2.2% of 226 subjects had an AHI < 1/h and EtCO₂ values ≥ 50 mmHg during ≥ 50% TST, with a mean %TST ≥ 50 mmHg of 2.8 ± 11.3, range 0.0–85.2.⁶ Together, these reports suggest that hypoventilation may occur in a small proportion of relatively healthy children in the absence of apneas and hypopneas. Because participants with AHI < 1 were not eligible for randomization in the CHAT study, we do not have outcome data for this group. Hypoventilation in the absence of elevated AHI may be an important subset of sleep disordered breathing that requires further study. Because children with asthma and obesity were included in this study, the hypercapnia in these patients may have been related to these or other health problems. Alternatively, this finding may be spurious, reflecting measurement error or night-to-night variability.

Analysis from our large and standardized dataset provides information useful in considering the range of values of EtCO₂ likely to be observed in a pediatric sleep laboratory. We found that although mean wake EtCO₂ values are commonly > 45 mmHg, criteria for hypoventilation were rarely met. Only 2 of 267 children (0.7%) had an awake EtCO₂ value > 50 mmHg. Our analysis showed a mean increase of EtCO₂ of 3.0 ± 1.7 mmHg between wake and sleep. This is consistent with previously reported values of 3- to 4- mmHg rise in EtCO₂ from wake to sleep states.^{3,7,17} We also observed that no child fulfilled the adult criterion for hypoventilation that requires a ≥ 10 mmHg increase in EtCO₂ to values > 50 mmHg, during sleep lasting at least 10 min.¹ Study strengths included the large sample, wide geographic and racial diversity, and use of standardized methods to assess baseline and follow-up characteristics, including use of a central sleep reading center and a randomized controlled design that allowed assessment of EtCO₂ responsiveness to surgery. The study was limited by the lack of follow-up data on children with a baseline AHI < 2/h, an exclusion criteria for the CHAT study.

CONCLUSION

This is the first randomized controlled trial on pediatric sleep disordered breathing that allowed extensive analyses of EtCO₂

values. Interpretable, very good EtCO₂ waveforms were available for 91% of children with suspected OSAS studied at accredited pediatric sleep laboratories following a standardized protocol, even in the presence of adenotonsillar hypertrophy. Five percent of children were observed to have hypoventilation in the absence of elevated AHI levels. Increasing AHI severity levels were associated with increased risk of hypoventilation, though the correlation was modest. Thus, in clinical practice, EtCO₂ can be anticipated to provide information that differs from other measures in a minority of children. The clinical applicability of this information, however, is not clear as the AHI, in comparison to EtCO₂, was more responsive to adenotonsillectomy, and neither AHI nor EtCO₂ predicted changes in cognitive and behavioral outcomes. However, the finding of elevations in EtCO₂ levels in African American children suggests the potential that this information may be helpful in better characterizing OSAS differences across subgroups of children. Further investigation with other outcomes will be needed to determine whether EtCO₂ monitoring provides outcome-relevant data among the 5% of children who have isolated elevations of EtCO₂ during assessment of sleep disordered breathing.

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APPENDIX

In a small substudy of 19 polysomnograms, when both the Novametric capnograph and BCI capnocheck were used, the following calibration equations were identified.

For BCI peak CO₂:

$$\text{Nova_est_CO}_2\text{PEAK} = (r \text{ CO}_2\text{peak} * 0.79956) + 9.17655$$

For BCI wake mean CO₂:

$$\text{Nova_est_CO}_2\text{BLWAKE} = (r \text{ CO}_2\text{blwake} * 0.65305) + 13.40939$$

For BCI sleep mean CO₂:

$$\text{Nova_est_CO}_2\text{BLSLP} = (r \text{ CO}_2\text{blslp} * 0.51229) + 20.03075$$

For BCI mean CO₂ in REM sleep:

$$\text{Nova_est_CO}_2\text{AVGR} = (r \text{ CO}_2\text{avgr} * 0.70253) + 10.67195$$

For BCI mean CO₂ in NREM sleep:

$$\text{Nova_est_CO}_2\text{AVGNR} = (r \text{ CO}_2\text{avgnr} * 0.49613) + 20.83379$$

For BCI percentage time CO₂ > 45 mmHg:

$$\text{Nova_est_PCT CO}_2\text{G45} = (\text{rpct CO}_2\text{g45} * 0.64525) + 7.67373$$

For BCI percentage of time CO₂ > 50 mmHg:

$$\text{Nova_est_PCT CO}_2\text{G50} = (\text{rpct CO}_2\text{g50} * 0.42979) + 0.64553$$