World Journal of Pediatrics (2018) 14:57–65
https://doi.org/10.1007/s12519-017-0108-4

ORIGINAL ARTICLE

Behavioral consequences of children with sleep-disordered breathing after adenotonsillectomy

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Received: 22 July 2016 / Accepted: 3 March 2017 / Published online: 20 February 2018

Abstract

Background Adenotonsillectomy (AT) has been an effective treatment for sleep-disordered breathing (SDB) in children, and several studies described the risk of postoperative weight gain and obesity in children treated with AT. The present study aimed to evaluate behavioral improvements in children with SDB one year after adenotonsillectomy and to investigate an influence of postoperative weight gain on behaviors.

Methods The study included 170 children aged 5–11 years who underwent adenotonsillectomy for SDB and 150 controls. Body mass index percentile was obtained for age and gender, and parental sleep-related breathing disorder (SRBD) questionnaire was used to assess the severity of SDB. Psychological assessment was performed pre- and post-adenotonsillectomy using standardized questionnaires including strength and difficulties questionnaire, children's depression inventory and screen for child anxiety-related emotional disorder.

Results The mean age of 170 patients was 7.7 ± 1.5 years with 73 (42.9%) girls and 97 (57.1%) boys. The mean follow-up period were 15.4 ± 2.7 months. The patients had shown significant improvements in SDB scores as well as in questionnaire-based behavioral problems after adenotonsillectomy. The odds of a child being overweight were significantly increased after adenotonsillectomy. Less improvements in hyperactivity and conduct problems were observed in the patients with older ages, higher SRBD scores, and overweight/obesity at 1-year follow-up after adenotonsillectomy.

Conclusion These data suggest that abnormal behavioral outcomes should be evaluated postoperatively, which potentially could be reduced with the early adenotonsillectomy and adequate postoperative weight control.

Keywords Obesity · Obstructive sleep apnea · Pediatric · Snoring · Tonsillectomy

Introduction

The prevalence of obstructive sleep apnea (OSA) in the pediatric population is currently estimated at 3% of all children and sleep-disordered breathing (SDB) has been reported around 12% of children [1–4]. Long-term adverse effects on the cardiovascular, neurocognitive, and somatic growth consequences are well characterized in childhood OSA. Regardless of the severity of symptoms, behavioral problems are relatively prevalent in children with OSA, and the lack of correlation between the severity index by polysomnography and neurobehavioral outcomes has been assumed to be due to the influence of other environmental and genetic interactions or insufficient sleep [5]. Recent evidence suggests that primary snoring, even in the absence of OSA, is associated with cognitive, behavioral, and various psychosocial problems, particularly for hyperactivity or schooling problems [2, 6–9].

Since adenotonsillar hypertrophy is a major determinant of SDB or OSA in pediatric population, the most effective first-line therapy has been adenotonsillectomy (AT). AT as one of the most common surgical procedures on children accounts for more than 500,000 procedures annually in the United States [10]. Although primary snoring has been known to be effectively treated by AT, it remains unclear whether AT also improves cognitive and neurobehavioral abnormalities as the previous studies have provided inconsistent results [11–13].

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In addition, several studies have described subsequent weight gain or the risk of childhood obesity after AT [14–17]. Various hypotheses have attempted to explain post-tonsillectomy weight gain, including decreased physical activity on restful sleep, decreased efforts of breathing, excessive caloric intake, less fidgety, increased levels of growth hormones, and decreased levels of systemic catecholamines. As the global epidemic of obesity has been issued among a pediatric population over the past few decades, obesity also became a great concern as a risk factor for developing OSA. The obesity rate of children aged 6–11 years in the United States revealed around 18% in 2012 [18], and the estimated prevalence of SDB was 36% in obese children [19, 20], which was much higher than the estimated prevalence of all children. Clinical features of OSA are more complex in obese children and markedly reminiscent of the typical presentation of OSA in adults, which often persist or recur after AT. We have previously reported that the presence of SDB in children is associated with a wide spectrum of behavioral problems using outpatient-based psychological screening tools [21]. Therefore, it would be important to understand a relationship between postoperative morbid obesity and behavioral consequences in children who had undergone AT.

The aim of the present study is to prospectively evaluate the improvements of emotional and behavioral problems in children with SDB before and one year after AT procedure and to investigate the behavioral influences of postoperative weight gain, along with any increased risk of obesity.

Methods

Study design and participants

A total of 220 pediatric patients aged 4–9 years, who were admitted prior to AT in the Sleep Disorders Center at CHA University Bundang Hospital between June 2013 and January 2014, were invited to complete standardized questionnaires. All were identified with a primary complaint of SDB with or without intermittent sleep apnea. The children with recurrent tonsillitis, chronic debilitating disease such as asthma, cranio-facial anomalies, neuro-muscular diseases, cognitive deficits, or any prior psychiatric diagnosis were excluded. Of these, 170 (77.3%) patients aged 5–11 years were available for the 1-year follow-up analysis and finally enrolled in the study. Prospective cohort study was performed. A total of 150 controls with similar age and sex of the patients were recruited through a public announcement without any health information except body height and weight. Parents/guardians were informed for the written consent on behalf of children, who gave verbal assents. The study was approved by the CHA University Bundang Hospital Ethics Committee.

Clinical assessments

Adenoid size was determined based on the A/N ratio of adenoidal depth (A) to nasopharyngeal diameter (N) on lateral radiograph [22]. Pathologic adenoidal hypertrophy was considered when A/N ratio was greater than 0.55. The tonsils were graded as follows: grade I = small tonsils confined to the tonsillar pillars; grade II = tonsils that extended just outside the pillars; grade III = tonsils that extended outside the pillars, but do not meet in midline; grade IV = large tonsils that meet in midline [23]. Allergen-specific immunoglobulin E blood test is performed. Baseline and postoperative body mass index (BMI) was calculated as weight (kg)/height (m^2), and each BMI value was standardized by conversion to percentile defined by corresponding age and gender [24]. Children were classified as underweight (BMI < 5th percentile), normal weight (BMI ≥ 5th and < 85th percentile), overweight (BMI ≥ 85th and < 95th percentile), or obese (BMI ≥ 95th percentile). Overnight polysomnography was performed in 90 children. For otherwise healthy children with a history consistent with nighttime snoring, restless sleep, daytime symptoms including somnolence, behavior changes, and poor cognitive performance as well as highly obstructing adenotonsillar hypertrophy on endoscopic examination, with or without witnessed apnea, were preceded with adenotonsillectomy without prior polysomnography. Standard sleep staging and event scoring were performed according to the pediatric guidelines of American Academy of Sleep Medicine [25]. Obstructive apnea was defined as the presence of continued inspiratory effort associated with a > 90% decrease in airflow for duration of ≥ 2 breaths. Hypopnea was defined as a ≥ 50% decrease in airflow for duration of ≥ 2 breaths associated with arousal, awakening, or reduced arterial oxygen saturation of ≥ 3%. Obstructive apnea was defined by the presence of an apnea/hypopnea index (AHI) ≥ 1 event per hour. The symptoms of sleep-disordered breathing (SBD) were assessed by a previously validated survey, the pediatric sleep questionnaire sleep-related breathing disorder scale (PSQ-SRBD), with higher scores indicating greater severity of illness [26]. Scores above 0.33 on overall score suggested a risk for SRBD.

Questionnaires-based study outcomes

All patients completed standardized questionnaires, which have been previously described in more detail [21], at enrollment before AT and 1 year after surgery.

Strength and difficulties questionnaire (SDQ)

The SDQ is a brief behavioral screening questionnaire with 5 subscales (emotional symptoms, conduct problems, hyperactivity/inattention, peer-relationship problems, and prosocial behavior) [27, 28]. The SDQ includes 25 items comprising 5 items for each subscale with a 3-point rating scale (0: not true; 1: somewhat true; 2: certainly true). The total difficulties score is obtained by simply summing up the scores of all questions of subscales except those related to prosocial behavior and can vary from 0 to 40 points. Total difficulties score of 14–16 was regarded as slightly raised score, which may reflect clinically significant problems and 17–40 as a substantial risk of clinically significant problem.

Children's depression inventory (CDI)

The CDI consists of 27 items scored on a three-point scale (0: absent; 1: moderate; 2: severe) reflecting the severity of cognitive, affective, and behavioral signs of depression [29, 30]. Overall CDI score ranges from 0 to 54 and higher scores imply the presence of more severe depression. A 22-point cut-off value indicates the threshold level discriminating children at the risk of depression from healthy children [30]. The internal consistency of the CDI in our sample was adequate with Cronbach's α of 0.80.

Screen for child anxiety-related emotional disorders (SCARED)

The SCARED has been shown effective in identifying the pediatric anxiety disorders [31, 32]. It contains 41 items of five factors including general anxiety, separation anxiety, social phobia, school phobia, and physical symptoms of anxiety using three-point scales (0: almost never; 1: sometimes; 2: often). Total and subscale scores are obtained by summing relevant items and a higher score reflects higher levels of anxiety. Score of 25 or greater indicate the presence of anxiety disorder. The internal consistencies of the SCARED subscales in our sample were generally satisfactory with Cronbach's α of 0.80 (somatic/panic), 0.75 (generalized anxiety), 0.82 (separation anxiety), 0.73 (social phobia), 0.60 (school avoidance), and 0.84 (total anxiety score).

Statistics

The data were analyzed using IBM SPSS Statistics Version 22. Internal consistencies were tested by Cronbach's alpha coefficient. Two group comparisons between patients and controls were made using Student's t tests or χ^2 tests. Multiple means were compared among groups as indicators of discriminant validity by two-way ANOVA analysis with repeated measures, followed by pair wise post hoc tests. A two-tailed Wilcoxon matched-pairs signed rank test was used to analyze the height%, weight%, BMI%, and PSQ-SRBD scores at baseline compared with the postoperative measure within the study group. Mcnemar test was applied to analyze the significance of the comparison of relative frequencies of psychiatric comorbidities between baseline and postoperative follow-up measures. Test results with $P < 0.05$ were regarded as statistically significant.

Results

Changes of growth pattern at 1-year follow-up

The mean age of 170 patients was 6.4 ± 1.6 years at enrollment and 7.7 ± 1.5 years at 1-year follow-up, respectively, with 73 (42.9%) girls and 97 (57.1%) boys. The mean follow-up after AT was 15.4 ± 2.7 months. The mean age of community controls was 7.6 ± 1.5 years at 1-year follow-up, with 65 (42.3%) girls and 85 (56.7%) boys. Demographic and clinical characteristics of the patients and controls are summarized in Table 1. There were no significant differences between patients and controls in age or sex ratio. No significant differences were found for parental socioeconomic status including maternal education level and household income between patients and controls.

Table 1 Participants characteristics

Variables	Patients (n = 170) 1-year follow-up	Controls (n = 150) 1-year follow-up
Age (y), mean ± standard deviation	7.7 ± 1.5	7.6 ± 1.5
Male gender, n (%)	97 (57.1)	85 (56.7)
Maternal educational level		
Less than high school, n (%)	6 (3.5)	4 (2.7)
Low economic status[a], n (%)	18 (10.6)	13 (8.7)

[a]Monthly household income < 1,500,000 Korean won. There were no significant differences between the study groups

AHI score in 90 patients at baseline was 15.6 ± 16.8. Symptoms of SDB for children who underwent AT were measured with the use of PSQ-SRBD scale, which showed a great reduction in the symptoms from 0.58 ± 0.19 at baseline, to 0.11 ± 0.12 at 1-year follow-up ($P < 0.01$).

Anthropometric data are presented in Table 2. There were no significant gender effects of the anthropometric variables. The results showed significant increases in both body height% and weight% in children who underwent AT, which led to significantly greater increases in BMI% and percentage of overweight after surgery, compared to community controls. No statistical differences were initially found in weight status between patients at baseline and controls. Fifty-five (32.4%) children were overweight or obese after surgery compared with 43 (25.3%) children before surgery (odds ratio = 10.58, 95% confidence interval = 6.18–18.13, $P < 0.01$). However, patients were no more likely to become obese at 1-year follow-up than they were before.

Individual baseline and follow-up data for height%, weight%, and BMI% are shown in Fig. 1. For younger children aged 5–8 years, the baseline height%, weight%, and BMI% seem to correlate inversely with the postoperative change in height%, weight%, and BMI%. However, for older children aged 9–11 years, the postoperative change in height% was relatively higher than that of weight% and BMI%, and these variables were not affected by baseline values.

Improvements of behavioral ratings after AT

Compared with community controls, preoperative children at baseline had significantly higher total scores on SDQ and SCARED scale (Table 3). In particular, subscale scores for emotional symptoms, conduct problem, and hyperactivity/inattention were significantly elevated. At 1-year follow-up after surgery, there were significantly greater improvements on average scores on total SDQ and total SCARED scales, which was close to the mean of community controls. In detail, the scores for subscales of emotional symptoms, conduct problem, and hyperactivity/inattention among SDQ were significantly improved in AT group. Subscale scores for separation anxiety, social anxiety, and significant school avoidance among SCARED were also significantly improved at 1-year follow-up. Scores for the CDI scale were reported generally too low to have discrimination power, with no differences between patients and controls. Gender-related differences were not observed.

Subgroup analyses

Psychiatric distress level of the patients was determined according to the previously validated cut-off points. The number of patients scored above cut-off points of total SDQ and SCARED scores was significantly reduced in the younger children group aged 5–8 years after AT (Fig. 2). However, no statistically significant differences were observed regarding pathologic total SCARED for the older children group aged 9–11 years, although similar improvements were proven for pathologic total SDQ scores. Detailed analysis of SDQ subscales revealed that the all subscales were effectively reduced for the younger children, whereas the older children tended to have persistent behavioral problems over almost all subscales except emotional subscales. Furthermore, the patients were divided into higher and lower scoring groups at the median postoperative PSQ-SRBD score of 0.12. The number of patients with pathologic total SDQ and total SCARED scores was significantly reduced in both groups (Fig. 3). However, in detailed analysis of SDQ subscales, the improvements of the subscales for the conduct problem, hyperactivity/inattention, and peer problem

Table 2 Anthropometric data before and after adenotonsillectomy for patients

Variables	Baseline		1-year follow-up	
	Patients (n = 170)	Controls (n = 150)	Patients (n = 170)	Controls (n = 150)
Height (cm), mean ± SD	121.4 ± 13.6	122.7 ± 13.9	128.3 ± 11.9	126.9 ± 12.8
Height percentile (%)[a], mean ± SD	53.3 ± 31.4	53.9 ± 31.0	65.8 ± 29.9[‡]	54.7 ± 30.6
Weight (kg), mean ± SD	26.0 ± 9.5	25.2 ± 10.9	29.9 ± 9.7	28.8 ± 10.0
Weight percentile (%)[a], mean ± SD	55.9 ± 30.1	54.6 ± 32.0	65.8 ± 27.2[‡]	56.4 ± 31.2
BMI (kg/m^2), mean ± SD	17.1 ± 3.0	16.8 ± 2.6	17.8 ± 2.7[‡]	17.2 ± 2.6
BMI percentile (%)[a], mean ± SD	57.1 ± 30.7	56.5 ± 29.6	61.3 ± 28.5[‡]	57.2 ± 30.4
Underweight (BMI < 5%), n (%)	11 (6.5)	8 (5.3)	0 (0)[‡]	7 (4.7)
Normal weight (5% ≤ BMI < 85%), n (%)	117 (68.2)	111 (74.0)	115 (67.6)	112 (74.6)
Overweight (85% ≤ BMI < 95%), n (%)	21 (12.4)	17 (11.3)	34 (20.0)[†]	16 (10.7)
Obese (BMI ≥ 95%), n (%)	22 (12.9)	14 (9.3)	21 (12.4)	15 (10.0)

[a]Height, weight, and BMI percentile were calculated by corresponding age and gender; significant differences are marked, [†]$P < 0.05$, [‡]$P < 0.01$. *BMI* body mass index, *SD* standard deviation

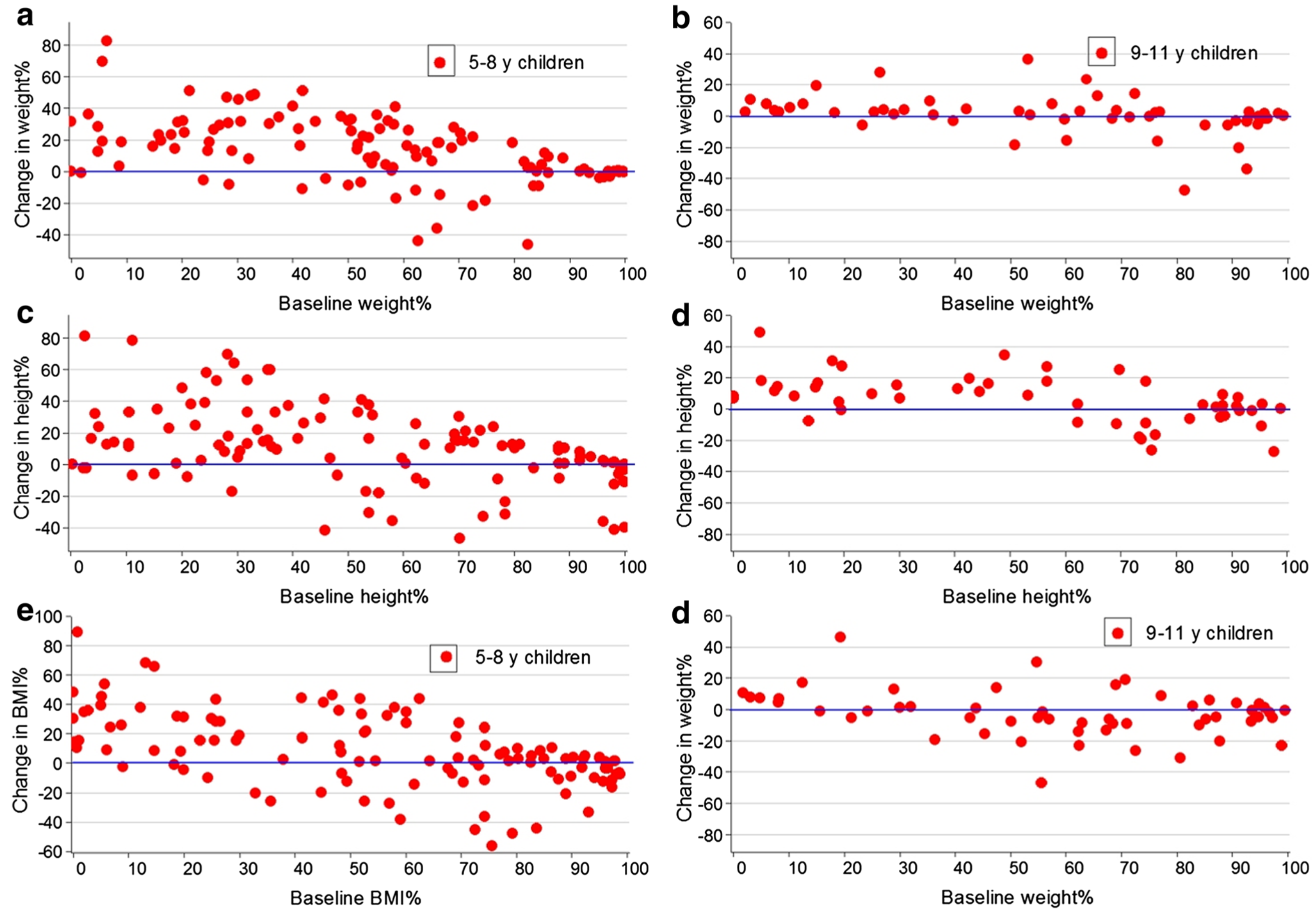

Fig. 1 Change in weight, height, and body mass index (BMI) percentile (%) as a function of baseline weight, height, and BMI% in 5–8 year and 9–11 year children

were less frequently observed in the higher PSQ-SRBD group than the lower PSQ-SRBD group. All participants experienced a significant reduction in the rate of pathologic total SDQ scores regardless of postoperative weight status (Fig. 4); however, the subscale for the conduct problem and hyperactivity/inattention was not improved in patients with overweight/obesity. In addition, there were no significant differences between pre and postoperative pathologic total SCARED scores in children with overweight/obesity.

No statistically significant differences were observed on pathologic CDI scores and there were no consistent relationships between questionnaires-based behavioral improvements and a tonsil or adenoid size or allergen-specific IgE levels.

Discussion

The most salient findings of this study are (1) that the increased risk of parent-reported adjustment difficulties on the SDQ and self-reported anxiety in children with SDB was successfully reduced with AT and long-term maintenance of improvements was achieved; (2) that children with SDB gained weight and the odds of a child being overweight were significantly increased after AT; and (3) that children with older ages, higher SRBD scores, and overweight/obesity at 1 year after AT are more likely to exhibit higher levels of hyperactivity and conduct problem.

Primary sleep disorders for children have been known to be associated with neuropsychological deficits and attention deficit hyperactivity disorder (ADHD), which are often reversed, but not all, upon treatments. Therefore, potential cognitive and behavioral improvements through AT have been of great concern to the management of OSA. Mechanism by which OSA elicits neural deficits remains unresolved, although it has been assumed that the sleep fragmentation and episodic hypoxia that characterize OSA might lead to alterations of the neurochemical substrates of prefrontal cortex [33–35]. SDB in children even in the absence of OSA appears to be associated with a wide spectrum of hyperactivity and social withdrawals [36]. The lack of strong correlations between OSA severity and neurobehavioral

Table 3 Post-operative 1-year behavioral ratings of the children with sleep-disordered breathing

Variables	Baseline		1-year follow-up	
	Patients (n = 170)	Controls (n = 150)	Patients (n = 170)	Controls (n = 150)
SDQ[a] scale				
Emotional symptom	3.2 ± 1.6[‡]	2.3 ± 1.4	2.5 ± 1.2	2.4 ± 1.5
Conduct problem	1.7 ± 1.4[†]	1.5 ± 1.2	1.4 ± 1.1	1.4 ± 1.2
Hyperactivity/inattention	3.2 ± 2.4[†]	2.5 ± 1.9	2.5 ± 1.8	2.5 ± 1.4
Peer problem	1.9 ± 1.7	1.4 ± 1.2	1.6 ± 1.3	1.4 ± 1.3
Prosocial behavior[a]	7.3 ± 2.0	7.4 ± 1.7	7.6 ± 1.5	7.4 ± 1.9
Total difficulties	10.0 ± 5.0[‡]	8.0 ± 3.8	8.1 ± 3.5	7.8 ± 3.8
CDI[a] scores	5.4 ± 4.3	5.0 ± 4.0	2.4 ± 2.5[a]	4.9 ± 4.1
SCARED[a] scale				
Panic disorder or significant somatic symptoms	2.2 ± 2.5	1.8 ± 2.5	1.9 ± 2.1	1.7 ± 2.3
Generalized anxiety	2.6 ± 2.9	2.3 ± 2.3	2.4 ± 2.3	2.5 ± 2.4
Separation anxiety	4.9 ± 3.3[†]	3.7 ± 3.3	3.7 ± 3.2	3.8 ± 3.2
Social anxiety	4.8 ± 3.5[†]	4.3 ± 3.3	3.8 ± 3.0	4.4 ± 3.0
Significant school avoidance	0.5 ± 1.0[†]	0.3 ± 0.7	0.4 ± 0.8	0.4 ± 0.7
Total scores	15.0 ± 10.3[†]	12.9 ± 9.0	12.2 ± 8.8	12.5 ± 8.9

Date are mean ± standard deviation. *SDQ* strength and difficulties questionnaire, *CDI* children's depression inventory, *SCARED* screen for child anxiety-related emotional disorders. [a]Prosocial subscale does not contribute to the total difficulties score; significant differences are marked, [†]$P < 0.05$, [‡]$P < 0.01$

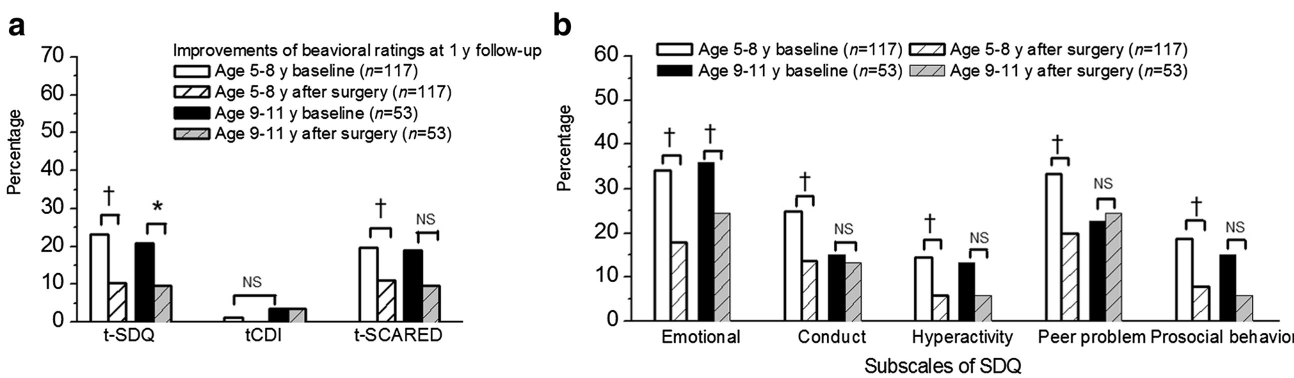

Fig. 2 Improvements of behavioral ratings numbers (%) of patients with significant pathologic scores between patients aged 5–8 years and patients aged 9–11 years at follow-up 1 year after adenotonsillectomy (**a**). Detailed analysis of SDQ subscales is provided (**b**). *SDQ* strength and difficulties questionnaire, *CDI* children's depression inventory, *SCARED* screen for child anxiety-related emotional disorders, *NS* not significant. *$P < 0.05$, †$P < 0.01$

consequences suggests that multiple factors that are most related to sleep quality rather than respiratory events are involved in its pathophysiology. Given the tendency for significant psychological distress over childhood to be associated with mental illness in adulthood, early recognition would be an important step to prevent long-lasting deleterious consequences.

As OSA has been reported to influence the somatic growth, AT might spur rapid weight gain and the risk of obesity in both normal weight and overweight children with or without OSA [14–17]. Although high behavioral and emotional difficulties as well as poor academic performances have been frequently observed among obese children [21, 37, 38], the influence of the obesity on behavioral consequences of children with OSA remains currently controversial [39, 40]. If excessive adiposity in children with SDB commonly occurs after AT, more attention should be paid not only to prevent a future recurrence of SDB symptoms but also to reduce adverse behavioral influences. However, there have been no studies evaluating

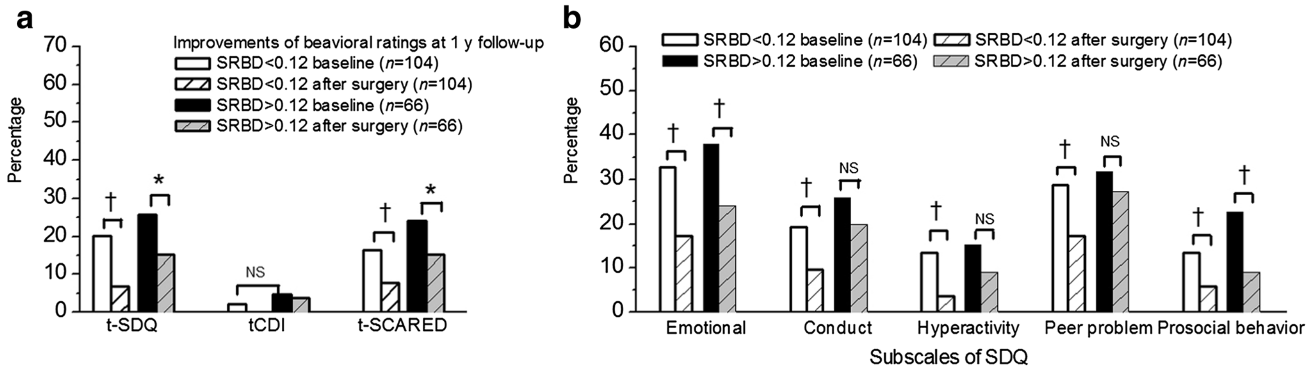

Fig. 3 Improvements of behavioral ratings at follow-up 1 year in children who underwent adenotonsillectomy. Numbers (%) of patients with significant pathologic scores in a group of patients divided by PSQ-SRBD scores (**a**). Detailed analysis of SDQ subscales is provided (**b**). *SDQ* strength and difficulties questionnaire, *CDI* children's depression inventory, *SCARED* screen for child anxiety-related emotional disorders, *PSQ-SRBD* pediatric sleep questionnaire sleep-related breathing disorder scale, *NS* not significant. *$P < 0.05$, †$P < 0.01$

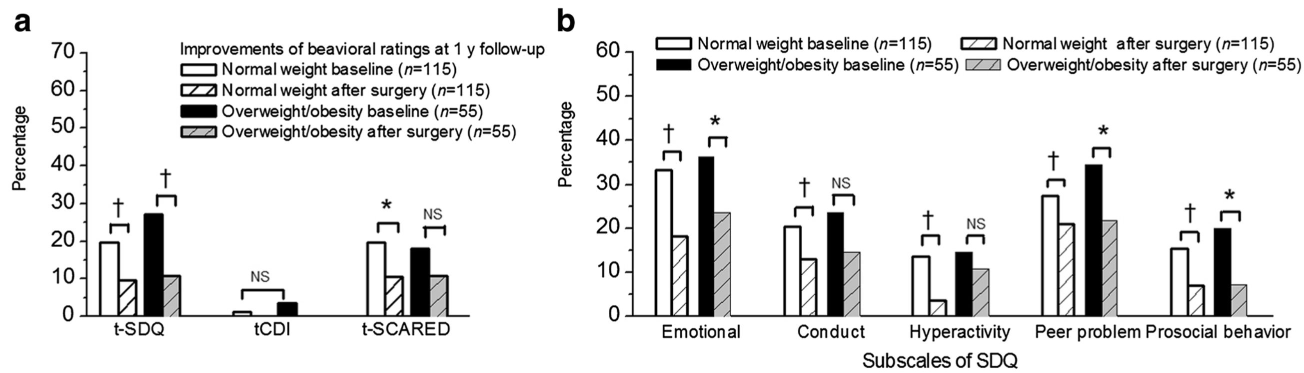

Fig. 4 Numbers (%) of patients with significant pathologic scores between normal weight patients and patients with overweight/obesity at follow-up 1 year after adenotonsillectomy (**a**). Detailed analysis of SDQ subscales is provided (**b**). *SDQ* strength and difficulties questionnaire, *CDI* children's depression inventory, *SCARED* screen for child anxiety-related emotional disorders, *NS* not significant. *$P < 0.05$, †$P < 0.01$

behavioral or psychological aspects of postoperative weight gain after AT.

Our results indicated that children who have undergone AT experienced an increase in weight percentile, BMI percentile, and percentage overweight. Before AT, the mean baseline BMI% was around the 57th percentile and percentage overweight in children with SDB was not greater than that of controls. After surgery, there was a significant increase in mean BMI% at 61th percentile. Catch up growth after AT was also demonstrated for children with failure to thrive. However, the change in BMI% was significantly less in children aged 9 years and older than younger children. It appears that early childhood around adiposity rebound upon age 5–6 years [41] might contribute to the development of excessive weight gain after AT. Because weight gain is a complex, multifactorial issue including behavioral, metabolic, and genetic factors rather than surgery itself, long-term monitoring the growth of surgically treated children for SDB would be necessary to determine the influence of AT on BMI.

The elevated level of emotional and behavioral difficulties such as conduct problem and hyperactivity were successfully reduced after AT. The younger children demonstrated greater postoperative improvements on pathologic behavioral ratings compared to the older children. It seems that the susceptibility to behavioral deficits in older children would be often affected by the environment factors, such as social interactions, which produces variable treatment responses. Furthermore, we observed better behavioral improvements in normal weight children than children with overweight/obesity postoperatively. ADHD has been known to affect approximately 3–7% of children and the prevalence of ADHD in children with snoring and/or sleep apnea has been generally reported two- to three-fold higher [42]. In the present study, the number of patients above pathologic hyperactivity scores was significantly decreased in children with normal weight after AT, whereas there were no significant interval changes in children with overweight/obesity postoperatively.

The present study has some limitations. Since the study specifically targeted to those who responded to the survey, the results may not generalize to entire postoperative population. In addition, since the behavioral data were collected at only one point in time, the long-term relationship between obesity, OSA, and behavioral problems in children who underwent AT would be the subject of ongoing research. The absence of polysomnography before and following adenotonsillectomy makes it difficult to know the degree of severity and reduction of OSA symptoms. The socioeconomic condition of urban children in the study also appears to affect mental illness. The purpose of the present study was not to determine a psychological diagnosis or causal relationship but to screen patients at high risk for behavioral or psychological distress to provide comprehensive evaluation and interdisciplinary therapeutic strategy. Our results confirm adverse behavioral effects of postoperative overweight/obesity and point that primary caregivers should be aware of the likelihood of the risk of unintentional weight gain after AT.

In conclusion, the present study indicates that impacts on emotional and behavioral problems in children with SDB could be ameliorated postoperatively if the symptoms of SBD were successfully reduced through AT. However, behavioral improvements, particularly on hyperactivity and conduct problem, were not consistently evident for overweight/obese children or children aged 9 years and older. It is conceivable that the appreciation of postoperative adequate weight control after early AT should be adapted to improve behavioral consequences.

Author contributions KJY designed and performed the study, and analyzed the data. KHM designed and performed the study, analyzed the data, and wrote the manuscript. LCH analyzed the data. All authors approved the final version of the manuscript.

Funding No funding was secured for this study.

Compliance with ethical standards

Ethical approval This study was approved by the hospital ethics committee.

Conflict of interest The authors have no conflicts of interest to disclose.

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