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Adenotonsillectomy can decrease enuresis and sympathetic nervous activity in children with obstructive sleep apnea syndrome

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Summary

Background
The nocturnal intermittent hypoxia caused by obstructive sleep apnea syndrome (OSAS) can provoke the sympathetic nervous activity (SNA). Salivary alpha-amylase (sAA) is a sensitive, non-invasive biomarker for reflecting the SNA, and a useful marker for pediatric OSAS subjects. Adenotonsillar hypertrophy (ATH) is the most commonly identified risk factor in OSAS childhood, therefore, several studies showed that the adenotonsillectomy (T&A) may alleviate nocturnal enuresis (NE) in children with OSAS.

Objective
The present study was to investigate the effect of T&A on NE, the change of sAA value in ATH and OSAS children, with/without NE, and with/without the operation.

Study design
37 children (Group A) were admitted for ATH and NE. The saliva samples were taken before and after polysomnography for the measure of sAA. After the T&A, the children were followed-up for 1 year. 35 OSAS children with NE but no T&A were as a NE watchful-waiting group (Group B), 32 subjects without OSAS or NE were as non-OSAS control (Group C), 42 cases who underwent T&A but did not have NE were admitted to evaluate the SNA (Group D). Follow-up included evaluations for NE, sAA and urinary catecholamine after the T&A or at the equivalent time points.

Results
The observational results in the present study showed a significant rate of the disappearance of NE 1 month after the T&A and had an almost complete resolution 1 year later. OSAS may irritate oxidative stress and increase SNA in pediatric subjects, which reflected by increased levels of sAA and urinary catecholamine, while the T&A can decrease enuresis and the SNA in children with OSAS (Figure).

Discussion
Little research has previously focused on the relationship between childhood OSAS and the SNA. No data are currently available regarding comparisons of sAA levels before and after the T&A in children with OSAS and enuresis. Our findings in this present study showed that there was a resolution or decrease in enuresis events and drops in sAA levels following T&A, which were consistent with earlier study. However, there was no significant difference in the urinary catecholamine levels was found between OSAS groups with or without NE. Furthermore, there was no correlation between the urinary catecholamine and polysomnography parameters.

Conclusions
T&A has a favorable therapeutic effect on NE and may decrease SNA in children with OSAS. sAA might be associated with instability of ANS by OSAS and have a consistent relationship with the apnea-hypopnea index. Our studying aims had been met.

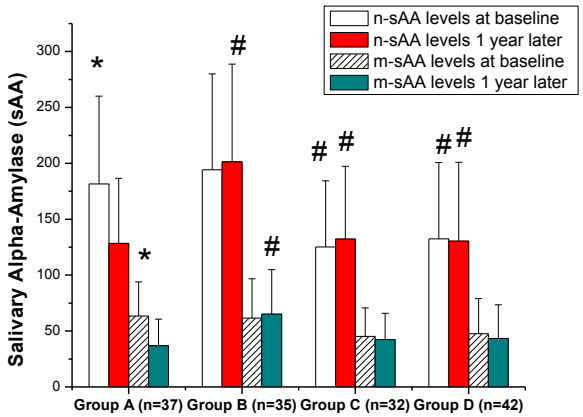

Figure Levels of n-sAA and m-sAA at baseline and 1 year later in 4 groups. # $P < 0.05$, compared with Group A or B. * $P < 0.05$, compared with Group A,C or D.

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a type of sleep-disordered breathing that is characterized by intermittent, partial or complete upper airway obstruction [1,2]. A peak incidence of this syndrome is in childhood at 2–8 years of age [3–5]. The most commonly identified risk factor is adenotonsillar hypertrophy (ATH) [6]; therefore, the definitive treatment is adenotonsillectomy (T&A) [2,6–8]. Numerous adverse health outcomes, including cognitive and behavioral deficits, are associated with OSAS [2]. Compared with adult cases, nocturnal enuresis (NE) is a relatively common finding in children [9]; it has been reported that as many as 47% of children with OSAS have NE [9]. Several studies have investigated NE in children with upper airway obstruction [9–12] and the effect of T&A [11–14]. Some reports have agreed that there is a resolution or decrease in enuresis events following T&A.

The nocturnal intermittent hypoxia caused by OSAS can activate oxidative stress and provoke sympathetic nervous activity (SNA) [15,16]. The elevated sympathetic tone is probably attributed to the increased risk of neurocognitive and cardiovascular events, and endocrine and metabolic comorbidity [17]. However, little research has previously focused on the relationship between childhood sleep-disordered breathing and SNA. Regulated by the sympathetic nervous system, salivary alpha-amylase (sAA) has been recommended as a sensitive, non-invasive biomarker for physiological stress-related changes in the body that reflect the SNA [18]. A growing body of resulting literature has consistently shown the validity and reliability of this emerging parameter, and been a useful marker for OSAS with pediatric subjects [19]. Furthermore, sampling for sAA is easy and pain-free to collect, and optimal for multiple sampling in children [19].

By understanding that the increasing SNA induced by hypoxia during OSAS could be represented by sAA, and that T&A may eliminate enuresis events in children with OSAS, it was speculated that the estimation of sAA might predict the presence and severity of SNA in children with NE who are diagnosed with OSAS. However, no data are currently available regarding comparisons of sAA levels before and after T&A in children with OSAS and enuresis.

Therefore, the present study compared the frequency of NE before and after T&A operation, with or without the procedure, in pediatric OSAS subjects with ATH. It also explored the change of sAA value in ATH and OSAS children, with or without NE, and with or without the operation.

Material and methods

Subjects

A total of 146 consecutive children, with a range of 5–9 years of age, who were examined at the sleep laboratory of the present institution between January 2011 and May 2015 were prospectively enrolled in this study. The Medical Ethics Committee of the Medical School at Wuhan University had approved the protocol for this study. Written informed consent was obtained from their parents.

Eligible children in Group A were those with OSAS caused by ATH and NE (at least 1 episode per week) with snoring or OSAS without prolonged oxyhemoglobin desaturation. They were first screened by a detailed clinical history and sleep questionnaire completed by each child's parents, a complete physical examination by a pediatric pulmonologist or an otolaryngologist, and confirmed by nocturnal polysomnography. Their family members consented to the T&A operation, the pre-operative polysomnography, and agreed to participate in the postoperative phase of this study.

Exclusion criteria included severe polysomnography findings with an apnea-hypopnea index $\geq$30 events/hour, or an obstructive apnea index $\geq$20 events/hour, or arterial oxyhemoglobin saturation of $<$90% for $\geq$2% of the total sleep time. All participants in the study received a full evaluation for secondary causes of enuresis. Children with enuresis caused by other systemic chronic medical conditions or those pharmacologically treated for NE were excluded from the study.

In the standard sleep questionnaire, parents were asked whether their child currently suffered from monosymptomatic or nonmonosymptomatic enuresis, and whether they had a dry period of at least 6 months; however, no daytime urinary symptoms were included. A total of 37 children met the inclusion criteria (OSAS + NE + T&A, Group A). To compare the frequency of NE and the change of sAA level, 35 OSAS children with ATH and NE but no T&A (their parents did not agree to the operation) were an NE watchful-waiting group (Group B, 13 cases with frequent NE and 22 with occasional NE). Another 32 subjects without OSAS (obstructive apnea-hypopnea index $<$2 or obstructive apnea index $<$1) or NE were a non-OSAS control (Group C). A further 42 cases who underwent T&A for simple ATH but did not have NE were also admitted into this study to assess the SNA (Group D). However, the pediatric or otolaryngologic interviewers did not know which group the subjects belonged to.

Polysomnography

Each child was taken to the sleep laboratory and overnight polysomnography was performed according to the standards of the American Thoracic Society [20]. The Sandman® Elite sleep diagnostic system (Puritan Bennett, Pleasanton, CA, USA) was used to record and analyze the variables. Sleep staging and arousals were scored according to the criteria of Rechtschaffen and Kales [21] and the American Academy of Sleep Medicine criteria [22,23]. The same investigator performed all scoring. Obstructive apneic and hypopneic events were scored according to the recommended pediatric criteria [22,23]. Obstructive apnea was defined as paradoxical breathing for $\geq$2 respiratory cycles, with complete cessation of inspiratory airflow. Hypopnea was defined as a reduction in the amplitude of respiratory effort of $\geq$50% from the sleeping baseline level, or a discernible reduction that did not reach the above criteria but was associated with at least a 3% decrease in arterial oxyhemoglobin saturation or an arousal. The apnea-hypopnea index was calculated as the average number of apneas and hypopneas per hour of sleep. OSAS was defined as an obstructive apnea-hypopnea index of $\geq$2 events/hour or an obstructive apnea index $\geq$1 event/hour [6,24].

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