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Original Article

Long-term changes in blood pressure control in elementary school-aged children with sleep-disordered breathing

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ABSTRACT

Objective: In adults sleep-disordered breathing (SDB) has been associated with impaired baroreflex control of blood pressure (BP), which has been linked to increased cardiovascular morbidity. In children, the long-term effects of SDB on baroreflex sensitivity (BRS) and BP variability (BPV) are unknown.
Methods: Children previously diagnosed with SDB ($n = 40$) and 20 nonsnoring controls aged 11–16 y underwent overnight polysomnography with continuous BP measurement, four years after the original diagnosis. At follow-up, SDB was categorized as resolved (absence of snoring and obstructive apnea hypopnea index (OAHI) $\leqslant 1$) or unresolved (continued to snore or had an OAHI > 1). BRS and BPV were calculated using cross-spectral analysis and power spectral analysis, respectively.
Results: Only children with resolved obstructive sleep apnea (OSA) at follow-up demonstrated an increase in BRS from 9.7 ± 3 (ms mmHg^{-1}) at baseline to 11.8 ± 4 (ms mmHg^{-1}) at follow-up ($P = .03$). However, children with all severities of both resolved and unresolved SDB showed a significant decrease in BPV from baseline to follow-up (a decrease in total power BPV ($P < .05$) and a shift in BPV spectra away from respiratory-related frequencies (increased low-frequency/high-frequency [LF/HF] ratio, $P < .01$). The change in OAHI was the sole determinant of change in BRS, HF power, and LF/HF ratio.
Conclusions: Improvement in SDB was associated with improved BP control, regardless if SDB was treated or spontaneously resolved four years after initial diagnosis. Our findings highlight the importance of monitoring children to ensure improvement of SDB and reduce the risk for cardiovascular morbidity in the future.

1. Introduction

Accumulating evidence suggests that sleep-disordered breathing (SDB) during childhood is associated with adverse effects on the cardiovascular system [1]. This finding is concerning as childhood SDB is common, with up to 35% of the pediatric population having *primary snoring* (PS) [2], a term that describes children who snore 3 or more nights per week but do not exhibit any gas exchange abnormalities or sleep fragmentation on polysomnography (PSG). Obstructive sleep apnea (OSA) is the most severe form of SDB and affects 1% to 5% [3] of children. In contrast to PS, OSA is characterized by snoring, intermittent hypoxia, hypercapnia or sleep disturbance. The association between childhood SDB and adverse cardiovascular effects also is concerning, as it is known that adults with SDB are at increased risk for hypertension, coronary artery disease and stroke [4,5]. Therefore, childhood SDB that persists into adulthood could potentially worsen the risk of adverse cardiovascular events.

Although the mechanisms underlying OSA-mediated cardiovascular morbidity are still being elucidated, it is known that obstructive breathing events are associated with increased sympathetic nervous system activation [6]. This finding in turn may contribute to the elevated blood pressure (BP) seen in both adults [7] and children [1] with SDB. Furthermore, sympathetic activation is believed to play a critical role in determining the sensitivity of the baroreflex in buffering BP fluctuations [8]. The baroreflex is key to BP homeostasis, as it is responsible for controlling short-term fluctuations of BP. This control is achieved through the detection of BP changes by stretch receptors in the walls of the carotid sinuses and aortic arch. Essentially, the baroreflex system provides negative feedback control to buffer BP changes through the modulation of heart rate (HR), cardiac contractility, and vascular resistance [8].

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Elevated BP as seen in SDB [1,9,10] can lead to remodeling of the carotid arterial wall making it less distensible, and this has been suggested as a potential mechanism for the baroreceptors to become activated less [11] or less sensitive to changes in BP. In support of this, adults with OSA have been shown to have depressed baroreflex sensitivity (BRS) [12]. Impaired BRS also results in increased BP variability (BPV), which is now being recognized as an independent cardiovascular risk factor [13] and has been linked to end-organ damage [14,15]. We [16] and others [17,18] have recently shown that children with OSA also demonstrated decreased BRS as well as increased BPV compared to nonsnoring controls during sleep. Although PS was not associated with decreased BRS compared to nonsnoring control children [16], studies in adults have shown decreased BRS in snoring individuals even in the absence of OSA [19,20]. Furthermore, children with PS show other effects on the cardiovascular system such as elevated BP and autonomic dysfunction similar to children with OSA. Hence the long-term effect of PS on BRS and BPV is currently unknown.

As the most common cause of childhood SDB is enlarged tonsils and adenoids, the usual treatment for more severe OSA is tonsillectomy (T&A). To date, few studies have assessed the effect of treatment of SDB on the cardiovascular system of children [21–25], and only one recent study has examined the effect of treatment on BRS and BPV [26]. Our study was a short-term follow-up of 6 months and included children with OSA and a control group but did not include any children with PS. Furthermore, the effect of untreated or persistent SDB on BRS and BPV has not been studied, and the long-term consequences of this disorder remain unknown. The aim of our study was to assess BRS and BPV in children with all severities of SDB and nonsnoring controls four years after diagnosis. We hypothesized that BRS would increase and BPV would decrease in those with resolved SDB and that children with persisting SDB would continue to show impaired BRS and BPV.

2. Methods

Participation in our study was voluntary and no monetary incentive was offered. Written informed consent was obtained from parents and verbal assent from the children on the night of the study. Approval was granted by Southern Health and Monash University Human Research Ethics Committees.

2.1. Participants and study design

Our study was a prospective follow-up study of children who were originally studied between July 2004 and December 2008 when they were aged 7–13 years. At the baseline study 155 children consisting of 116 who had been referred for assessment of suspected SDB and 39 nonsnoring control participants recruited from the community, were studied. Our study began in 2009 and aimed to follow-up children who had a BP recording during sleep at baseline after a time frame of four years. Therefore, children without an adequate BP recording at baseline or those originally studied in 2004 were excluded, leaving 135 children ($n = 99$ SDB, $n = 36$ control) eligible to participate. Of those 135 children, 16 were not able to be contacted. The remaining 119 children were invited to participate in the study and those who agreed to participate underwent repeat overnight PSG together with completion of a number of questionnaires to assess their quality of life and sleep habits and quality. Treatment type (if any) received for SDB after initial diagnosis was documented via parental report on the night of the follow-up study. Treatment was not standardized as part of the study and reflected the clinical decision of the treating physician and parents. Smoking status and history of high BP for parents of participants also were documented on the night of the study. The sleep and respiratory outcomes from the follow-up study have been published [27].

2.2. Protocol

Prior to the PSG study anthropometric measures including height and weight were recorded and body mass index (BMI) was calculated and converted to *z* scores [28]. Participants underwent routine overnight pediatric PSG in the Melbourne Children's Sleep Centre using a commercially available PSG system (either Series S or Series E Sleep System, Compumedics, Melbourne, Australia at baseline, and Series E Sleep System at follow-up). The following signals were recorded: electroencephalography (Cz, C4-A1, C3-A2, O2-A1, O1-A2), left and right electrooculogram, submental electromyogram (EMG), left and right anterior tibialis muscle EMG, electrocardiogram. Oxygen saturation (SpO_2) was measured using Masimo Radical®SET (Masimo Corp., CA, USA) at baseline and the Bitmos GmbH, (Dusseldorf, Germany) at follow-up, both of which use Masimo signal extraction technology for signal processing. All oximeters were set to a 2-s averaging time. Transcutaneous carbon dioxide was measured at baseline using a TCM4/40 (Radiometer, Copenhagen, Denmark) and at follow-up using a TINA TCM3 (Radiometer, Copenhagen, Denmark). Respiratory parameters recorded included thoracic and abdominal respiratory inductance plethysmography (Pro-Tech zRIP™ Effort Sensor, Pro-Tech Services Inc., Mukilteo, WA, USA), nasal pressure (Salter Style®, Salter Labs, Arvin, CA, USA) and oronasal airflow (Sandman®BreathSensor™, Child Airflow Thermistor, Tyco Healthcare, UK). The children went to bed once lead application was complete and were awakened at 0600.

In addition to standard PSG, BP was continuously measured and noninvasively via finger arterial photoplethysmography using a Finometer™ device (Finapres Medical Systems, Amsterdam, Netherlands). Finometer™ BP measurements were validated by comparing values with at least three simultaneous measurements of office BP performed with an aneroid sphygmomanometer (Big Ben Reister, Rudolf Riester, Jungingen, Germany) at baseline and Dinamap (V100, CARESCAPE™, Freiburg, Germany) at follow-up, using an appropriately sized cuff. Comparison of BP measurements were made with the participant lying supine during quiet wakefulness. All Finometer™ measurements were within 5 mmHg of the Office BP measurements. Wake BP was measured while the participant was lying quietly in bed prior to lights out for a minimum of 10 min. BP recording was continued throughout the night while participants were asleep.

2.3. PSG data analysis and groups

All PSG studies were sleep-staged in 30 s epochs by experienced pediatric sleep technologists, with respiratory and sleep parameters being scored and calculated using the same protocol as previously published for the baseline study [9]. Data were excluded if <4 h of sleep were recorded. As the initial PSG studies had been conducted before the implementation of the American Academy of Sleep Medicine new scoring rules [29], all PSG studies were sleep-staged using Rechtshaffen and Kales criteria [30] into wake after sleep onset (WASO), nonrapid eye movement sleep stages 1, 2, 3 and 4 (NREM1–4), and rapid eye movement (REM) sleep. Sleep technologists scored the follow-up study blinded to previous SDB severity. Respiratory events were scored if they were $\geqslant 2$ respiratory cycles in duration, and the classification of apneas and hypopneas was based on the American Academy of Sleep Medicine criteria [31] with minor modifications in accordance to clinical practice at the time of the baseline study. Arousals were scored as either cortical arousals as defined by the American Sleep Disorders Association [32] or as subcortical activations [33]. Subcortical