Sleep Medicine Reviews 18 (2014) 179–189

Contents lists available at SciVerse ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Blood pressure regulation, autonomic control and sleep disordered breathing in children

Lauren C. Nisbet, Stephanie R. Yiallourou, Lisa M. Walter [a], Rosemary S.C. Horne [*,a]

The Ritchie Centre, Monash Institute of Medical Research, Monash University, Melbourne, Australia

ARTICLE INFO

Article history:
Received 20 December 2012
Received in revised form
10 April 2013
Accepted 29 April 2013
Available online 12 July 2013

Keywords:
Blood pressure
Obstructive sleep apnoea
Sleep disordered breathing
Primary snoring
Paediatric
Autonomic
Heart rate
Cardiovascular
Baroreflex

SUMMARY

Sleep disordered breathing (SDB) ranges in severity from primary snoring (PS) to obstructive sleep apnoea (OSA). In adults, SDB is associated with adverse cardiovascular consequences which are mediated, in part, by autonomic dysfunction. Although SDB is common in children, fewer paediatric studies have investigated these cardiovascular effects. Initial research focused on those with OSA, indeed children with PS were occasionally utilised as the comparison control group. However, it is essential to understand the ramifications of this disorder in all its severities, as currently the milder forms of SDB are often untreated. Methodologies used to assess autonomic function in children with SDB include blood pressure (BP), BP variability, baroreflex sensitivity, heart rate variability, peripheral arterial tonometry and catecholamine assays. The aim of this review was to summarise the findings of paediatric studies to date and explore the relationship between autonomic dysfunction and SDB in children, paying particular attention to the roles of disease severity and/or age. This review found evidence of autonomic dysfunction in children with SDB during both wakefulness and sleep. BP dysregulation, elevated generalised sympathetic activity and impairment of autonomic reflexes occur in school-aged children and adolescents with SDB. The adverse effects of SDB seem somewhat less in young children, although more studies are needed. There is mounting evidence that the cardiovascular and autonomic consequences of SDB are not limited to those with OSA, but are also evident in children with PS. The severity of disease and age of onset of autonomic consequences may be important guides for the treatment of SDB.

Introduction

Sleep disordered breathing (SDB) is a common disorder of childhood which ranges in severity from primary snoring (PS) to obstructive sleep apnoea (OSA). OSA affects 1–5% of children[1] and is characterised by prolonged partial and/or intermittent complete upper airway obstruction which disrupts normal ventilation and sleep patterns.[2] Occurring in 3–15% of children,[3] PS describes snoring without associated gas exchange abnormalities or sleep disruption. Despite differences in aetiology, SDB in both adults and children is associated with a number of negative outcomes, including autonomic and cardiovascular dysfunction (for reviews, see[4–10]). In adults there is a dose–response relationship between SDB severity (including snoring) and blood pressure (BP) levels,[11] but this association is less well described in children. In this review we will explore the relationship between autonomic dysfunction and SDB in children, paying particular attention to the influences of disease severity and/or age.

Autonomic control of heart rate and blood pressure in healthy children

The autonomic nervous system (ANS) plays a major role in homeostasis. The two divisions of the ANS, the parasympathetic nervous system and sympathetic nervous system, innervate similar organs but have opposing effects, and thus different outcomes are effected by a shift in the balance of the two systems. The cardiovascular system in particular is highly regulated by the ANS. Parasympathetic neurons innervate the heart, whilst sympathetic efferents innervate blood vessels, the heart, kidneys and adrenal medulla.[12] Parasympathetic activation slows heart rate (HR) through the vagus nerve, and has a rapid response time,[13] whilst sympathetic activation occurs more slowly and acts to increase HR.[14] Alongside HR, the ANS also determines BP through its control of cardiac output and vascular resistance.[12] Tight, short-term control of BP is effected by both parasympathetic and sympathetic

* Corresponding author. The Ritchie Centre, Level 5, Monash Medical Centre, 246 Clayton Road, Clayton 3168, Victoria, Australia. Tel.: +61 3 9594 5474; fax: +61 3 9594 6811.
E-mail address: rosemary.horne@monash.edu (R.S.C. Horne).
[a] Co-senior authorship.

1087-0792/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.smrv.2013.04.006

Abbreviations

ABP	ambulatory blood pressure
ANS	autonomic nervous system
AHI	apnoea hypopnoea index
BMI	body mass index
BP	blood pressure
BPM	beats per minute
BPV	blood pressure variability
BRS	baroreflex sensitivity
CI	confidence interval
DBP	diastolic blood pressure
ECG	electrocardiogram
HF	high frequency power
HR	heart rate
HRV	heart rate variability
LF/HF	low frequency to high frequency ratio
LF	low frequency power
MBP	mean blood pressure
MS	moderate-severe
NREM	non-rapid eye movement sleep
OAI	obstructive apnoea index
OAHI	obstructive apnoea hypopnoea index
OSA	obstructive sleep apnoea
PAT	peripheral arterial tonometry
pNN50	number of pairs of adjacent R–R intervals that differ in length by more than 50 ms
PS	primary snoring
PSG	polysomnography
PTT	pulse transit time
RDI	respiratory disturbance index
REM	rapid eye movement
SBP	systolic blood pressure
SDB	sleep disordered breathing
SpO_2	oxygen saturation
SWS	slow wave sleep

systems through the feedback loop of the baroreflex. Increases in arterial pressure are offset by a reduction in HR, leading to restoration of BP. Conversely, decreases in arterial pressure, or activation of chemoreceptors by hypoxia or hypercapnia, activate the baroreflex mechanisms resulting in increased HR and restoration of normal BP levels. This reflex can be actively reset to adjust to prolonged low or high BP as needed, for example with certain behaviours such as exercise. Baroreceptor resetting may also occur with cardiovascular disease and hence plays a role in the development of prolonged hypertension, as is associated with SDB in adults.[6] Decreased baroreceptor sensitivity leads to increased sympathetic activation, whilst conversely, prolonged raised sympathetic activity can result in attenuated baroreceptor sensitivity.[15] Also part of the sympathetic response, the adrenal glands react to stress (such as hypoxia or hypotension) by releasing catecholamines directly into the circulation, with the effect of redistribution of blood flow through the chronotropic and inotropic effects on the heart.[7]

Normal development of autonomic control of heart rate and blood pressure during childhood

HR and BP are the most common and easily assessed clinical indicators of autonomic function. Beat-by-beat HR can be measured non-invasively through an electrocardiogram (ECG). HR decreases during childhood; from age 5 to 18 y mean 24 h HR has been shown to reduce by 18 bpm in boys (92–74 bpm) and 15 bpm (93–78 bpm) in girls.[16] In contrast, systolic BP (SBP) increases with age,[16,17] whilst diastolic BP (DBP) increases slightly[17] or does not change with age.[16] BP is furthermore affected by body size and gender. In infants and toddlers, an increase in height of 30 cm was associated with a SBP and DBP increase of 10 mmHg.[18] A study of children and adolescents aged 5–21 y showed a slight but significant increase in SBP with height, which was more pronounced in boys than in girls.[19] SBP has been independently correlated with age, height and obesity, whilst in contrast DBP was reported to be independent of age and height and only weakly associated with obesity.[16] Gender differences in BP were apparent in children older than 11 y or of a height greater than 140 cm[16]; but were not apparent in younger children.[16,18,20]

BP can be measured non-invasively at a single point in time (clinic BP), intermittently over 24 h (ambulatory BP (ABP) monitoring) or continuously beat-by-beat through devices commonly worn on the finger. Interpretation of ABP monitoring requires the definition of day (wake) and night (sleep), of which the standard definitions are day-time as 8 AM to 8 PM and night-time as midnight to 6 AM. Wake and sleep periods are difficult to define in young children due to day-time napping and periods of wakefulness overnight. Parent-reported nap-time was associated with a day-time dip in BP in children aged 3–6 y.[20] The degree of change in BP from wake to sleep, referred to as nocturnal dipping, increases with increasing age.[18–20] The mean decrease in SBP and DBP was 3–6% and 3–11% respectively in infants aged 2–3 mo,[18] 8–10% and 16–18% in children aged 3–6 y,[20] and 13% and 23% in children aged 5–21 y[19]; the latter demonstrated dipping independent of height.

Normative BP values expressed as percentiles or z-scores, based on gender, age and height are published for clinic BP during wakefulness.[17,21–23] Normative values are also available specifically for ABP monitoring for day- and night-time periods and across 24 h, based on studies of German children aged 5–21 y.[16,19] No normative BP values are available specific to sleep states or stages, nor for continuous BP measurement. Measures of coupling between spontaneously occurring parallel fluctuations in BP and heart period increased with age in subjects aged 7–22 y, reaching a peak in adolescence.[24] This increase occurred despite a gradual decline in carotid artery elasticity, thus indicating an improvement in cardiovagal function with age.[24]

Oscillations in HR and BP occur over a 24 h period, and include fast changes lasting seconds as well as slower variations over minutes or hours.[12] Fluctuations in HR and BP, that is heart rate variability (HRV) and blood pressure variability (BPV), can be measured using beat-to-beat recordings of HR and BP respectively. HRV and BPV are commonly measured through time-domain and frequency-domain analyses.[25,26] Time-domain parameters are generally reflective of parasympathetic activity, and include measurements such as the number of pairs of adjacent R–R intervals of the ECG that differ in length by more than 50 ms (pNN50) for HRV,[25] and analysis of adjacent pulse intervals for BPV. The differences in speed of action of the parasympathetic and sympathetic nervous systems mean that the divisions operate at different frequencies. Frequency-domain HRV and BPV analysis, or power spectral density analysis, delineates the power within the low frequency (LF) and high frequency (HF) ranges of the HR and BP recordings.[25,27,28] The HF component is related to respiration (respiratory sinus arrhythmia) and thus reflects parasympathetic activity. The LF component of HRV measures a combination of sympathetic and parasympathetic activity, as mediated through the