Sleep-Disordered Breathing In Obese Children. Mecanisms, Diagnosis and Management

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In order to develop normally, children spend long hours of the day sleeping, around 12-13 hours/day for pre-schoolers (age 3-5 years), 10-11 hours/day for school-aged (age 5-10 years) and 8-10 hours/day for adolescents (age 14-16 years). Although all the functions of sleep remain unfully understood, sleep is vital for *restoration of body systems, energy conservation, brain development and memory consolidation, as shown by the adverse effects caused by sleep deprivation.*

During sleep, the respiratory system, including control of breathing, control of respiratory muscles and respiratory mechanics, meets challenging conditions. Sleep-disordered breathing (SDB) may occur as a consequence of imbalance between the different forces controlling the adjustment of breathing during sleep. SDB comprises a wide spectrum of sleep-related breathing abnormalities, among which obstructive sleep apnoea syndrome (OSAS) that is defined as the presence of obstructive apneas or hypopneas caused by recurrent obstruction of the upper airway during sleep, and obesity-hypoventilation syndrome (OHS) that is defined as the association of obesity and chronic daytime hypercapnia ($PaCO_2 \geq 45$ mmHg) in the absence of other causes of hypoventilation [1-2].

OSAS is by far the most common form of SDB. In the general population, the prevalence rate of OSAS is estimated to be at 2% of the children, with a peak incidence between 2 and 8 years. The main cause is enlarged tonsils and adenoids. Unrecognized and untreated OSAS may affect nearly every major system, causing daytime fatigue, growth delay, cardiovascular dysfunction, behavior disorders, cognitive impairment, etc... [1-4]. In obese children, SDB encompasses OSAS and OHS. Obesity is recognized as an important risk factor for OSAS. It significantly affects its clinical presentation and its management scheme. OHS is thus far rarely reported in obese children but its prevalence is likely to be underestimated [5-8].

The present chapter focuses on the clinical aspects of SDB in children with common obesity and provides an overview on mechanisms, diagnosis and management. Aspects regarding syndromic or genetic obesity will not be addressed.

Mechanisms For SDB In Obese Children

The pathophysiological factors underlying OSAS can be grossly divided into anatomical factors that reduce upper airway internal calibre and those that control upper airway opening. OSAS occurs when factors that aim to maintain upper airway open are overwhelmed by those that obstruct or close the airway during sleep. Therefore, partial or total obstruction of upper airway may result in obstructive apneas or hypopneas (i.e. cessation or reduction of the airflow, respectively), subsequent periods of desaturation (defined as decrease of the oxygen saturation) over the night, sometimes associated with hypercapnia and sleep disruption [2].

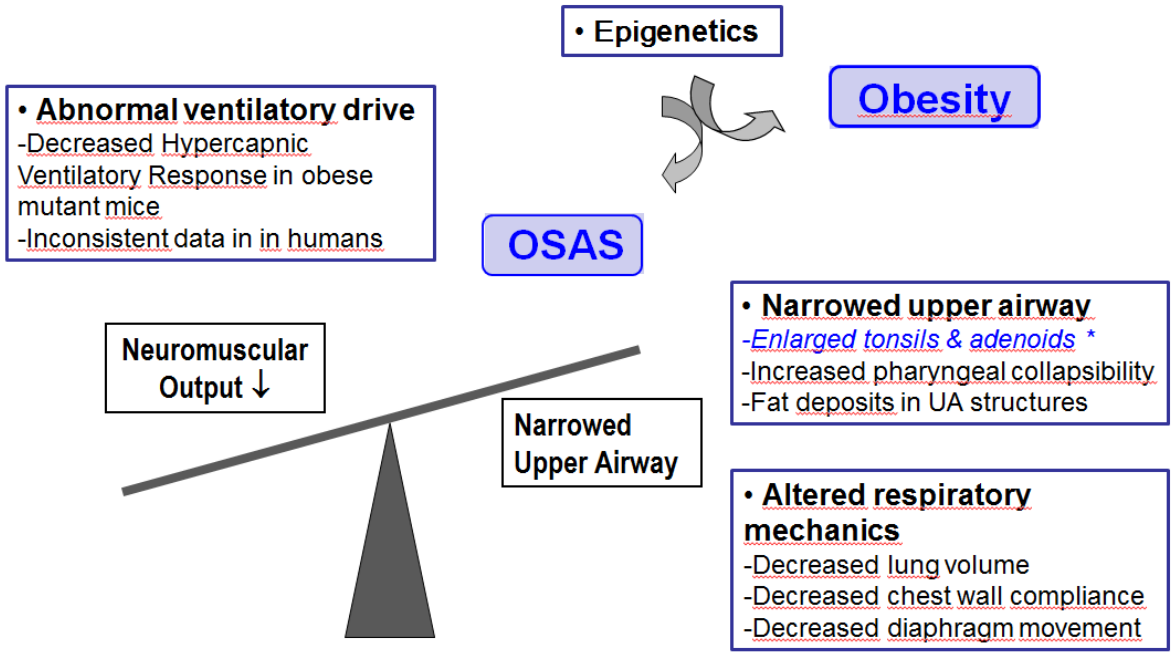

FIGURE 1. Multiple mechanisms involved in OSAS in the obese. Whereas enlarged tonsils and adenoids are the main cause found in the non-obese child, a number of additional factors likely contribute to generating OSAS in the obese.

In normally-weighted children, narrowed upper airway during sleep is mainly caused by anatomical obstacles such as large tonsils or adenoids. Figure 1 shows a number of additional factors thought to combine, further promoting OSAS in the obese. First, increased pharyngeal collapsibility, fat deposition in the subcutaneous tissue surrounding the airway in the cervical region, which reduces its internal caliber, laryngeal dysfunction-produced expiratory braking during sleep may contribute to an even more severe obstruction of the upper airway in the obese [9-13]. Second, obesity-related alterations in respiratory mechanisms further prompt impairment of gas exchange in case of disordered breathing. Restriction of lung volumes is mainly at the expense of functional residual capacity and expiratory reserve volume [14-15]. Fat deposition in the subcutaneous tissue surrounding the thorax and abdomen decreases chest wall compliance, increases intra-abdominal pressure, both factors limiting diaphragmatic excursion, thus producing shallow tidal breathing and increased work of breathing. Third, abnormalities of the central control of breathing have been demonstrated in mutant obese mice. Data remain inconsistent in humans, with studies showing decreased, unchanged or increased ventilatory responses to chemical stimuli [16-18]. Finally, one may hypothesize the role of epigenetic factors as obesity and OSAS share a number of candidate genes involved in the regulation of many pathways, metabolism, energy homeostasis, control of respiration and arousals [17-18]. However, the degree of responsibility of each of these factors in generating OSAS in the obese is more difficult to determine and requires further investigation.

Obesity is not associated in a straightforward manner with OSAS [13,19]. Worldwide studies show that not all obese subjects develop OSAS. This phenomenon suggests that susceptibility of the obese to OSAS may depend on individual physiological responses to obesity-induced physiological changes. Interestingly, a recent study shows that obese adolescents with OSAS exhibit a much less vigorous genioglossus muscular activity during sleep than those without OSAS, thus preventing the upper airway remain open [20]. Obese adolescents with OSAS or without OSAS have increased ventilatory responses to hypercapnia during wakefulness when compared to lean controls. However, during sleep, obese adolescents with OSAS show lower changes in response to hypercapnia of minute ventilation, inspiratory flow and inspiratory volume compared to those without OSAS. The authors hypothesized that central drive may play a significant role in adapting ventilation to hypercapnia [21].

OHS occurs when obesity is associated with daytime alveolar hypoventilation. In most of the cases, daytime hypoventilation comes in addition to chronic sleep hypoventilation caused by severe OSAS. In rare cases, it may involve predominantly altered central drive of breathing [5-8].

Obese Children are more exposed to SDB

Epidemiological studies show that obesity, defined as a body mass index (BMI) higher than 28 kg/m^2, increases the risk for OSAS by 4-5 times in a group of 399 children aged 2-18 years. Beyond a normal BMI adjusted for age and gender, increases of 1 kg/m^2 of the BMI increase the risk for OSAS by 12% and increase the number of apneas and hypopneas per hour of sleep by 3%. In the Cleveland Children Sleep and Health Study including 850 children from 8 to 11 years of age, the black American ethnicity is an additional risk for OSAS of 4-6 times in obese children. The presence of large tonsils in obese younger children, and a BMI higher than the 95th percentile in obese adolescents are predictors of significant OSAS [22-23].

Although obesity is recognized as a risk factor for OSAS, the real prevalence of OSAS remains difficult to determine in this specific population when considered as a whole. Early studies found that 24 to 60% of the obese children suffer from OSAS. However, these studies mostly included mono-center and/or small samples of patients, the latter being often referred for suspected respiratory disorders or having a morbid obesity (defined as a BMI >30 kg/m^2 or weight >180% of the ideal weight) [24-26].

More recently, studies aiming to determine the prevalence of OSAS use community-based samples of obese children. A cross sectional prospective, multicenter study included 245 children (3-14 years of age, BMI higher than 95ème percentile adjusted for age and gender). Their mean age was 10.8 ± 2.6 years and BMI 28.0 ± 4.7 kg/m^2. Using a cut-off value for presence of OSAS as an apnea-hypopnea index ≥ 3 /h of total sleep time, the prevalence rate was found at 21.5% [27].

Presentation of SDB in Obese Children

A constellation of clinical symptoms are suggestive of OSAS. Those found in obese children are not different from those in the non obese. Mechanisms underlying these symptoms are not equivocal. Moreover, a number of obesity-related co-morbidities may be associated (neurobehavioral, cardiovascular, metabolic disorders, etc…), thus further resulting in difficulties for the interpretation [28-29]. It is not uncommon that clinical symptoms are neglected or underestimated by children and their families, and often do not constitute reasons for consultation for most obese children. Therefore, it is important to search systematically in all children referred for obesity.

Typically, nocturnal and diurnal symptoms may be present in children suffering of OSAS. Parents most frequently report nocturnal snoring, sometimes notice periods of labored breathing type mouth breathing or breathing pauses followed by large movements of respiratory resumption and arousals. Nocturnal sweating and secondary enuresis are sometimes noticed. Night sleep can be agitated and restless, with nighttime awakenings. The morning awakening is slow, sometimes with headaches. There is a tendency for fatigue and daytime sleepiness, for behavioral problems or learning difficulties, type attention or memory deficit.

Scores calculated from sleep questionnaires are shown not to predict the presence of OSAS, neither do they correlate with its severity. Larger neck circumference was found in obese children with OSAS than in those without it [23]. Waist-to-height ratio has been shown to distinguish OSAS from habitual snoring in obese children [30]. Presence of large tonsils is a strong predictor for OSAS. In contrast, lung function tests performed during wakefulness contribute poorly to prediction of OSAS. Awake sitting and supine respiratory resistance was found increased in most obese children; nevertheless they were associated neither with the presence nor with the severity of OSAS [31].

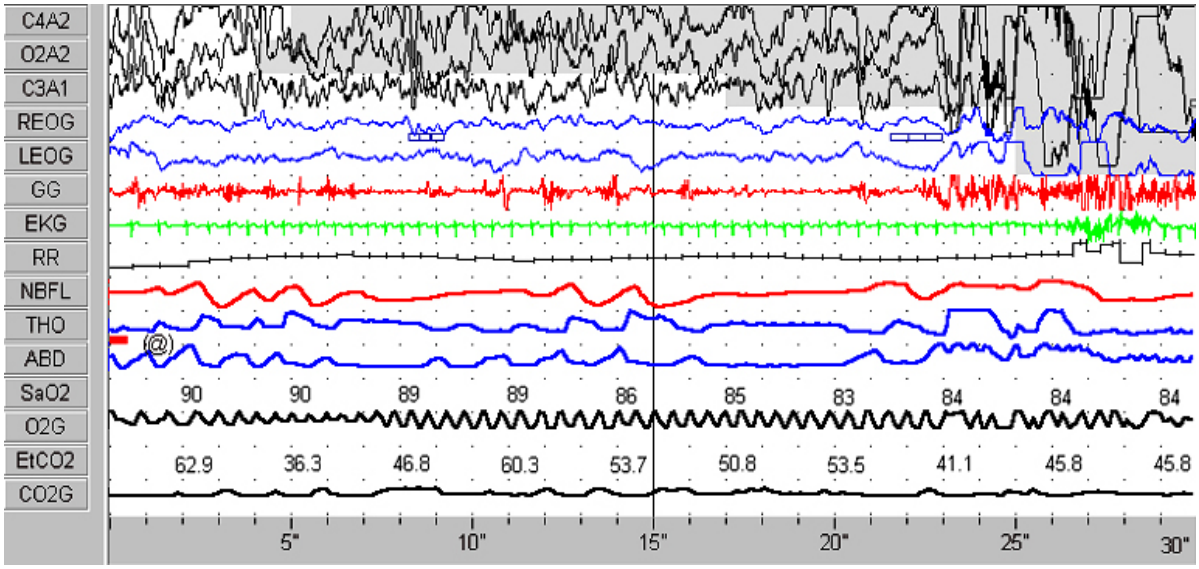

FIGURE 2. Polysomnographic tracing showing repeated obstructive apnoeas during sleep, associated with respiratory muscles recruitment, desaturation, hypercapnia, bradycardia and micro-arousals. *From top to bottom : C4A2/O2A2/C3A1, electroencephalogram ; REOG, LEOG, right and left electro-oculograms ; GG, genioglossus electromyogram ; EKG, electrocardiogram ; RR, cardiac period ; NBFL, naso-buccal airflow ; THO, ABD, thoracic and abdominal respiratory movements ; SaO_2, oxygen saturation measured using pulse oximetry ; O2G, plethysmographic signal of SaO2 ; $EtCO_2$, end-tidal CO_2 ; CO2G, signal of capnography.*

The key examination for diagnosis of OSAS is polysomnography (PSG). PSG is a test that simultaneously records neurophysiological parameters (electroencephalogram, electrooculogram, genioglossus electromyogram), respiration (airflow using pressure transducer and naso-oral thermistor, thoracic and abdominal respiratory movements, oxygen saturation using pulse oximetry, transcutaneous or end-tidal PCO_2) and heart rate over a night period performed in a sleep centre. OSAS is confirmed by an increased obstructive apneas-hypopneas index (OIAH) (defined as the number of apneas and hypopneas per hour of total sleep time). Obstructive apnoea is a cessation of airflow associated with persistent or increased respiratory efforts (Figure 2). Hypopnoea is a decrease in the amplitude of the airflow associated with desaturation and/or arousal. Apnoeas and hypopnoeas occur predominantly during rapid eye movement sleep (Figure 3). A flow limitation breathing pattern may be caused by partial upper airway obstruction and is associated with the recruitment of accessory respiratory muscles. Respiratory efforts are evidenced by increased amplitude of out-of-phase respiratory movements of the thorax and the abdomen. Repetitive obstructive apnoeas or hypopnoeas may induce oxygen desaturation, and sometimes alveolar hypoventilation (hypercapnia). Sleep may be disrupted by frequent respiratory event-induced arousals or awakenings throughout the night (Figure 4). PSG not only allows identification of OSAS, but also assessment of its severity.

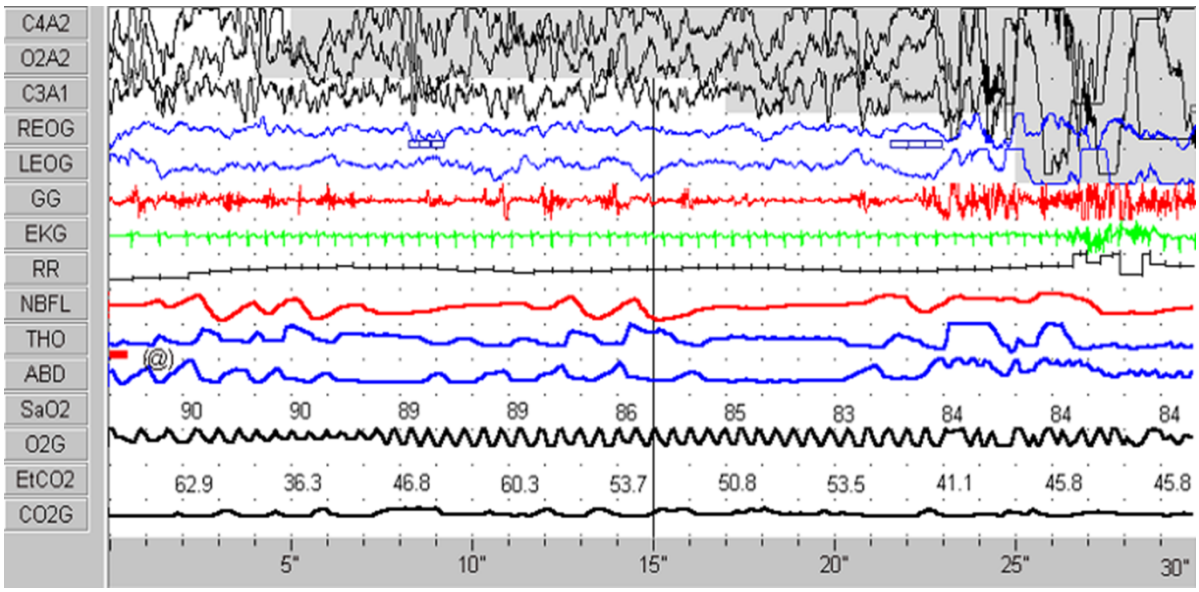

FIGURE 3. Two obstructive apnoeas associated with out-of-phase respiratory movements of thorax and abdomen, desaturation, hypercapnia and movement arousals. *See figure 2 for definitions of channels.*

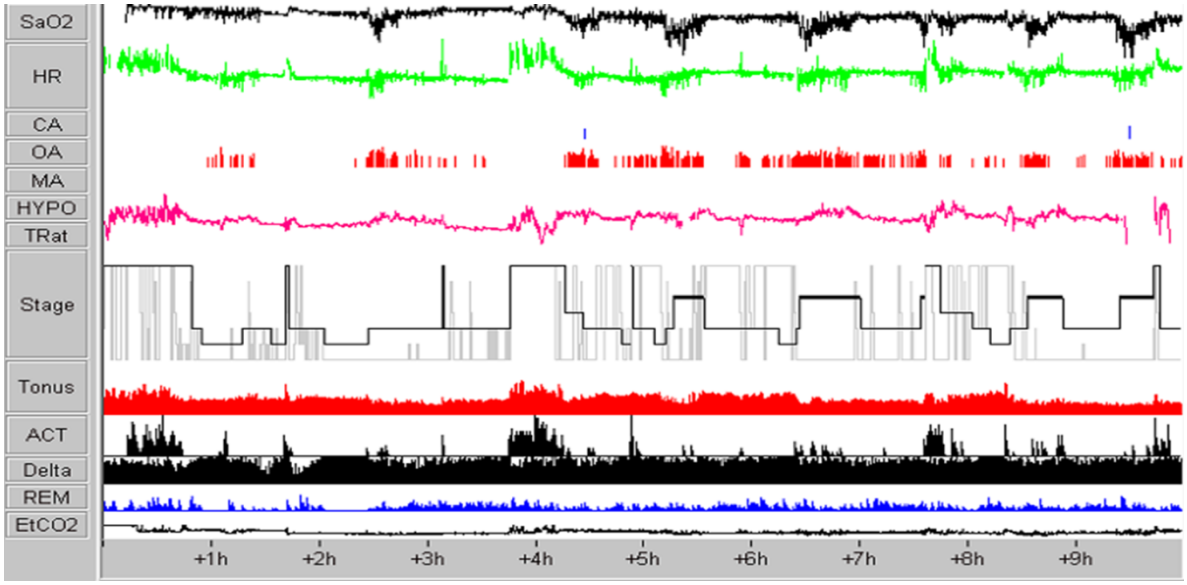

FIGURE 4. Sleep data of one night showing the occurrence of many obstructive apnoeas-hypopnoeas, concomitant desaturation, and frequent awakenings during sleep. *From top to bottom: SaO_2, oxygen saturation; HR, heart rate; CA, central apnoea; OA, obstructive apnoea; MA, mixed apnoea, Stage of sleep; ACT, actimetry; REM, rapid eye movement sleep; $EtCO_2$, end-tidal PCO_2.*

Some PSG-based studies reported that the degree of obesity correlates with the apnoea index and inversely correlates with the lowest value of oxygen saturation during sleep. Mean end-tidal PCO_2 was found to be higher in children with a more severe obesity (body weight higher than 200% of its ideal value) than in the others. However, no significant correlations exist between PSG-based variables (respiratory event indices, percent of sleep time with oxygen saturation lower than 90%, percent of sleep time with end-tidal PCO_2 higher than 50 mm Hg, arousal indices) and BMI, or age or gender [7,14,24-27].

OSAS in obese children differ in many aspects from that in obese adults. Excessive daytime somnolence which is a hallmark of obese adults with SDB is rarely noticed in obese children. Sleep latency objectively measured by the multiple sleep latency tests is found to be normal in obese children with OSAS [32-33].

More recently, a study reported the utility of a portable recording device for screening OSAS in a group of 25 obese adolescents [34]. These devices only record respiratory parameters (airflow, respiratory movements, and oxygen saturation) and heart rate. They do not record neurophysiological parameters, therefore sleep data are not available. The validity and effectiveness of these partial diagnostic tools are yet to be determined in larger sample of patients.

OHS with daytime hypercapnia is a clinical presentation found in a number of obese adults (xxx), but has been reported in a few obese children only [5-8].

The exploding rate of obesity in children worldwide in the last decades has dramatically impacted the prevalence of SDB worldwide. These results in an increase in the prevalence of morbidities associated with obesity, including metabolic, cardiovascular and respiratory diseases.

Management of SDB in Obese Children

Management of obese children with OSAS must be comprehensive. Co-morbidities should be identified and treated. Weight loss is the primary goal and depends on complying with dietary hygiene. In a study performed in a group of children and adolescents with severe obesity (mean BMI z-score 2.7), weight loss achieved during 5 months resulted in a reduction of BMI z-score by 0.9 and significantly decreased the severity of OSAS [35]. Tonsillectomy and/or adenoidectomy may be recommended if tonsils and/or adenoids are hypertrophied, but may induce a certain increase in BMI. Postoperative complications are more frequent in obese children than the non-obese, largely secondary to mechanical problems. Postoperative hospital surveillance is recommended in severely obese children. Adenoido-tonsillectomy has been shown to be effective in obese children with OSAS, however the rate of OSAS relapse is higher than in normally-weighted children [36-40]. When weight loss is not possible or in case of persisted OSAS after tonsillectomy, noninvasive ventilation on nasal mask continuous positive airway pressure has proved its feasibility and effectiveness to normalize gas exchange. It can be conducted in the child's home, under control by a specialized pediatric team [1,7].

Conclusion

Obesity increases prevalence of SDB in children and affects outcomes. Polysomnography is the key examination for identifying SDB and rating its severity. Weight loss should be the main objective, associated with tonsillectomy and/or non-invasive ventilation.

Management of obesity in children should include identification and treatment of SDB. A body of evidence is now available showing that sleep duration shortening and sleep fragmentation induced by SDB not only negatively impact on daytime vigilance and cognitive function, but may in turn favor obesity and its maintenance [41-42].

Abbreviations

AHI, apnoea-hypopnoea index;

BMI, body mass index;

OAHI, obstructive apnoea-hypopnoea index;

OHS, obesity-hypoventilation syndrome;

OSAS, obstructive sleep apnoea syndrome;

SDB, sleep-disordered breathing

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