Sleep Medicine 16 (2015) 625–630

Contents lists available at ScienceDirect

Sleep Medicine

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

Original Article

Impact of obesity on cognitive outcome in children with sleep-disordered breathing

Ottavio Vitelli [a], Alessandra Tabarrini [a], Silvia Miano [b], Jole Rabasco [a], Nicoletta Pietropaoli [a], Martina Forlani [a], Pasquale Parisi [a], Maria Pia Villa [a,*]

[a] Neuroscience, Mental Health and Sense Organs Department, Paediatric Sleep Disorder Centre, Faculty of Medicine and Psychology, La Sapienza' University, Rome

[b] Sleep and Epilepsy Center, Neurocenter of Southern Switzerland, Civic Hospital of Lugano, Switzerland

ARTICLE INFO

Article history:
Received 2 September 2014
Received in revised form 15 December 2014
Accepted 15 December 2014
Available online 7 February 2015

Keywords:
Obesity
Sleep-disordered breathing
Children
Cognitive impairment

ABSTRACT

Objectives: The objective of this study was to evaluate the impact of obesity on cognitive impairment, in children with obstructive sleep apnoea (OSA), children with OSA and obesity, and in normal controls.
Methods: Thirty-six children with OSA (group 1), 38 children with OSA and obesity (group 2) and 58 normal controls (group 3) were studied. The Total intelligence quotient (T-IQ), Verbal IQ (V-IQ) and the Performance IQ (P-IQ) scores were obtained using the Wechsler Intelligence Scale for Children – Third Edition Revised. All participants' parents filled out the questionnaire containing the attention deficit and hyperactive disorder rating scale to investigate symptoms of hyperactivity and attention deficit. Obese and non-obese children with sleep-disordered breathing (SDB) underwent polysomnography.
Results: T-QI and P-QI scores were significantly lower in group 2 with higher performance impairment at the subtest compared to other groups. In obese children, V-IQ was significantly correlated with age of onset ($r = 0.335$, $p = 0.05$) and duration of SDB ($r = -0.362$, $p = 0.02$), while P-IQ and T-IQ were correlated with body mass index (BMI) percentile ($r = -0.341$, $p = 0.03$) and respiratory disturbance index (RDI) ($r = -0.321$, $p = 0.05$), respectively. RDI and BMI negatively influenced T-IQ in obese children with OSA. No correlation was found between sleep parameters and IQ scores or subtest scores in all groups.
Conclusions: Obese children with OSA showed higher cognitive impairment. Obesity has an additive and synergic action with that exerted by OSA, speeding up the onset of complications.

1. Introduction

Sleep-disordered breathing (SDB) is a common condition in children that includes the broad spectrum of pathology ranging from primary snoring to obstructive sleep apnoea (OSA) syndrome. OSA in children is a "disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns" [1]. Symptoms include habitual snoring, apnoea, restless sleep and diurnal neurobehavioural problems, such as attention deficit and hyperactive disorder (ADHD), learning problems, behavioural disorders, and hypersomnolence [2–4]. Findings from previous research suggest that intermittent hypoxia during sleep and sleep fragmentation are the main causative factors involved in the pathogenesis of neurocognitive impairment of SDB [3–9].

Recently, the results of the Childhood Adenotonsillectomy Trial (CHAT) were published, and they clearly confirmed that neurocognitive and behavioural dysfunctions in children with OSA are consistent and partially reversible [10]. CHAT was a multicenter, single-blind, randomized, controlled trial in seven academic paediatric sleep centres in the USA designed to evaluate the efficacy of early adenotonsillectomy in comparison with watchful waiting with supportive care, with respect to cognitive, behavioural, quality-of-life and sleep factors in children with OSA, including obese children, during seven months of follow-up. As compared with a strategy of watchful waiting, surgical treatment for the OSA syndrome in school-age children did not significantly improve attention or executive function as measured by neuropsychological testing, but it did reduce symptoms and improve secondary outcomes of behaviour, quality of life, and polysomnographic findings.

Most studies have failed to find a direct correlation between SDB severity and cognitive and behavioural problems [11,12]. No direct dose–response relationship seems to exist between disease severity and cognitive outcomes. This has led to the hypothesis that other factors such as genetic susceptibility, environmental influences, and co-morbid conditions, such as obesity, shortened sleep duration and the presence of other sleep disorders, may also influence neurocognitive

* Corresponding author. Sleep Disorder Centre, Sant'Andrea Hospital, Via Grottarossa 1035-1039, 00189 Rome, Italy. Tel.: +390633775855; fax +390633775941.
E-mail address: mariapia.villa@uniroma1.it (M.P. Villa).

http://dx.doi.org/10.1016/j.sleep.2014.12.015
1389-9457/

outcomes. A prospective non-randomized study of children undergoing a diagnostic assessment for SDB, compared to normal controls, demonstrated that the ADHD rating scale scores were higher in children with SDB, and the intelligence quotient (IQ) estimate lower, with significant correlations with sleep microstructure, analysed by a cyclic alternating pattern (CAP) and cardiorespiratory parameters [13]. These data confirmed that other factors during sleep may influence the cognitive outcome in OSA children.

Obesity is considered one of the most important risk factors for OSA [14,15], and preliminary evidence suggests that it is an independent contributor to cognitive functioning [16]. One study demonstrated that the Performance IQ (P-IQ) score was markedly lower in overweight/obese patients than in those with normal weight, with a significant positive correlation between the P-IQ score and body mass index (BMI) [17]. OSA in the context of obesity may independently or synergistically affect neurocognitive function and maturation.

The aim of this study was to evaluate the effect of obesity on the neurocognitive disability of children with OSA, measuring IQ, and ADHD symptoms in children with OSA, in children with OSA and obesity and in normal controls.

2. Methods

2.1. Subjects

Children with SDB undergoing their first diagnostic assessment for OSA in our Paediatric Sleep Centre (Rome, Italy) were consecutively enrolled between January 2013 and December 2013. Patients with a history of any systemic diseases or major neurological or psychiatric disorders (such as autism, epilepsy, and headache), previous treatment for OSA (including tonsillectomy and adenoidectomy or orthodontic treatment), acute or chronic cardiorespiratory or neuromuscular diseases, dysmorphism, and major craniofacial abnormalities were excluded. Patients with a familial history of major neurological or psychiatric disorders, any type of mental retardation or known genetic syndromes were also excluded.

A detailed personal and family history was obtained for all the participants and a clinical examination was performed. Moreover, parents were asked when their child started to present nighttime symptoms (like snoring apnoea and restless sleep). Disease duration was defined as the time between onset of symptoms and our evaluation.

Body weight was determined to the nearest 0.05 kg, and height was measured to the nearest 0.1 cm using standardized measuring equipment. The measurements were taken in the morning after urination, with patients in only their underwear. BMI was calculated in kilograms per square meter and then converted to a sex- and age-specific BMI percentile value. Children were categorized using standard BMI-growth curves for age and gender criteria according to International Obesity Task Force (IOFT) cut-off points. Children underwent a laboratory polysomnography (PSG) in our sleep centre after one night of adaptation.

Age- and sex-matched control children were also recruited from two schools in the same urban area of the study groups. They were of Caucasian origin and of middle socio-economic status. The inclusion criteria were as follows: normal healthy prepubertal children had normal sleep habits; none of the controls was obese or had any serious physical, neurological or psychiatric disorder. No history of sleep problems (snoring, apnoeas, and restless sleep) were reported, as demonstrated by the negative Brouillette score [18], and none was taking medication at the time of testing. The control group underwent only cognitive assessment.

Moreover, we analysed the parental educational score. This score was calculated by summing mother and father instruction scores, using the following parameters: did not complete primary school = 1; completed primary school = 2; completed middle school = 3; dropped out of high school = 4; completed high school = 5; dropped out of university = 6; and completed university = 7.

The local ethics committee approved the study protocol, and all children's parents gave their informed consent to the procedures.

2.2. Cognitive assessment

IQ was obtained using the Wechsler Intelligence Scale for Children – Third Edition Revised (WISC-R, 1973; Rubini and Padovani, 1986), an intelligence test validated for children between the age of 6 and 16 years, usually requiring 75–80 min for its administration.

The test comprises 10 core subtests and two supplemental tests. These subtests generate a full scale score, Total IQ (T-IQ), and two composite scores known as indexes: the Verbal IQ (V-IQ), (including Vocabulary, Similarities, Comprehension, Information, Arithmetic, and Digit Span as a supplemental test) and the P-IQ, (including Block Design, Picture Stories, Picture Completion, Puzzle, Coding and Mazes as a supplemental test). The IQ testing was performed in the morning before the sleep study. A Wechsler score <70 was considered to indicate mental retardation, while a Wechsler score <85 was considered to indicate borderline intellectual functioning, according to the Statistical Manual of Mental Disorders, Fourth Edition, axis II diagnosis (1994).

All participants' parents filled out the questionnaire containing the ADHD rating scale [19], a clinical interview that recognizes symptoms of hyperactivity and inattention according to the Diagnostic and Statistical Manual of Mental Health Disorders, Fourth Edition. It consists of 18 items, divided into two subgroups of nine questions that investigate inattention and hyperactivity symptoms. Our purpose was to investigate symptoms of hyperactivity and the presence of attention deficit rather than diagnose ADHD syndrome.

2.3. Polysomnographic parameters

All patients underwent a full-night PSG in our sleep centre after one night of adaptation. Standard overnight PSG recordings were obtained using a Grass Heritage polygraph. The variables recorded included the following: a six-channel electroencephalogram (bilateral frontal, central temporal and occipital monopolar montages referred to the contralateral mastoid); an electrooculogram (electrodes placed 1 cm above the right outer canthus and 1 cm below the left outer canthus and referred to A1); and a submental electromyogram and electrocardiogram (one derivation). Sleep was subdivided into 30-s epochs, and sleep stages were scored according to the standard criteria of the AASM [20]. The following conventional sleep parameters were measured: total sleep time, defined as the time from sleep onset to the end of the final sleep stage; sleep efficiency, defined as the percentage ratio between total sleep time and total recording time (from lights-out clock time to lights-on clock time); and wakefulness after sleep onset, defined as the time spent awake between sleep onset and the end of sleep. The percentage of total sleep time in each stage was measured as follows: percentage of stage N1, stage N2, stage N3 and rapid eye movement (REM) sleep.

Respiratory events were counted according to the criteria established by the AASM [21].

Obstructive apnoea was scored when there was a ≥ 90% drop in the signal amplitude of airflow for at least the duration of two breaths during baseline breathing, associated with the presence of respiratory effort throughout the entire period of absent airflow. Central apnoea was defined as the absence of airflow, with the cessation of respiratory effort, lasting >20 s or lasting at least two missed breaths (or the duration of two baseline breaths), associated with an arousal, an awakening or a ≥ 3% desaturation; central apnoea occurring after gross body movements or after sighs was not