Neuropsychiatric Disease and Treatment

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ORIGINAL RESEARCH

# Depressive symptoms and childhood sleep apnea syndrome



This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment
22 August 2012
Number of times this article has been viewed

Marco Carotenuto[1]
Maria Esposito[1]
Lucia Parisi[2]
Beatrice Gallai[3]
Rosa Marotta[4]
Antonio Pascotto[1]
Michele Roccella[2]

[1]Sleep Clinic for Developmental Age, Clinic of Child and Adolescent Neuropsychiatry, Second University of Naples, Naples, Italy; [2]Child Neuropsychiatry, Department of Psychology, University of Palermo, Palermo, Italy; [3]Unit of Child and Adolescent Neuropsychiatry, University of Perugia, Perugia, [4]Department of Psychiatry, "Magna Graecia" University of Catanzaro, Catanzaro, Italy

**Background:** The relationship between sleep and mood regulation is well known, and some reports suggest a key role of sleep-related breathing disorders (SRBD) in the development of the symptomatology of depression, even if no conclusive data are actually found in the clinical literature. The aim of this study was to assess the relationship between SRBD and depressive symptoms in a population of school-aged children.

**Methods:** The study population comprised 94 children affected by SRBD and 107 healthy children. To identify the severity of SRBD, an overnight respiratory evaluation was performed. All subjects filled out the Italian version of the Children Depression Inventory (CDI) to screen for the presence of depressive symptoms.

**Results:** The group with SRBD showed higher CDI scores than the group without SRBD, with a positive correlation found between CDI scores, apnea-hypopnea index, and oxygen desaturation index values. Logistic regression showed that an apnea-hypopnea index $\geq 3$ and an oxygen desaturation index $\geq 1$ could be risk factors for development of depressive symptoms. According to receiver-operating characteristic curve analysis, the cutoff point for the apnea-hypopnea index that could cause a pathological CDI score ($\geq 19$) was $>5.66$, and the cutoff point for the oxygen desaturation index was $>4.2$. The limitations of this study are that our data are derived from one single psychometric test and not from a complete psychiatric evaluation, and our subjects came from a small group in southern Italy.

**Conclusion:** Our results suggest the importance of mood assessment in children affected by SRBD.

**Keywords:** depression, sleep-related breathing disorders, cardiorespiratory monitoring, children

## Introduction

Depression in childhood is a disabling condition associated with increased psychosocial and physical morbidity and mortality.[1,2] Early-onset depression in particular seems to be characterized by pervasive dysfunction throughout life.[3,4] In fact, depression during childhood and adolescence represents a significant public health concern, affecting about 1%–2% of prepubertal children and about 3%–8% of adolescents,[5–7] accompanied by a poor psychosocial outcome, multiple comorbid conditions, and a high risk of suicide and substance abuse, suggesting the necessity of early diagnosis and treatment. Moreover, early onset depression increases the risk of subsequent depressive episodes later in adolescence and adulthood, ranging from 45% to 72% over 3–7 years.[8,9] Because of the high costs associated with pediatric depression, the past 10 years has seen a growing interest in its prevention.[10] A link between mood dysfunction and sleep is also known and well established,[11,12] and includes difficulties such as falling asleep,[13,14]

Correspondence: Marco Carotenuto
Sleep Clinic for Developmental Age, Clinic of Child and Adolescent Neuropsychiatry, Via Sergio Pansini 5 PAD XI, 80131 Naples, Italy
Tel +398 1566 6988
Fax +398 1566 6694
Email marco.carotenuto@unina2.it

fragmented sleep,[15] symptoms of hypersomnia,[16] and sleep-related breathing disorders (SRBD).[17]

SRBD are disorders of breathing during sleep characterized by prolonged partial upper airway obstruction, intermittent complete or partial obstruction (obstructive apnea or hypopnea), or both prolonged and intermittent obstruction that disrupts normal ventilation during sleep, normal sleep patterns, or both.[18] In general, SRBD seems to play a key role in the symptomatology of depression, especially in adulthood,[19–21] even if the causal mechanism remains unclear. In fact, it is unknown if depression in patients with obstructive sleep apnea syndrome could be considered the primary consequence or if it occurs secondary to symptoms related to obstructive sleep apnea syndrome (eg, sleepiness, sleep problems, irritability, social withdrawal), or to other factors related to the syndrome (eg, obesity, hypertension).[22–25] Moreover, depressive symptoms are so frequent in adults affected by the syndrome that the current recommendation in these circumstances is that the mood disorder should be considered as secondary to the medical disorder and not as a distinct psychiatric entity.[22,25]

In 2004, O'Brien et al suggested that the link between different grades of SRBD and behavior could be exemplified by the effects of primary nocturnal snoring as a trigger of neurobehavioral deficits, such as attention-deficit hyperactivity disorder symptoms, social problems, and symptoms of anxiety and/or depression in children.[26] On the other hand, a clinical study shows that children with SRBD tend to have more internalizing symptoms,[27] such as anxiety and depressive traits, but without a specific explanation for the putative causal role of SRBD. The aim of this study was to assess the prevalence of symptoms of depression in a school-aged population of children affected by SRBD.

# Materials and methods

## Participants

The study population comprised 94 children with SRBD (49 males and 45 females, mean age 10.15 ± 2.60 years) consecutively recruited between January 2011 and May 2012 from the Sleep Clinic for Developmental Age at the Second University of Naples. Exclusion criteria were psychiatric illness (ie, schizophrenia, psychosis, attention-deficit hyperactivity disorder), mental retardation (IQ $<$ 75), neurological disorder (epilepsy, neuromuscular disorders, cerebral palsy), overweight (body mass index $\geq$ 85th centile) or obesity (body mass index $\geq$ 95th centile), and referral for sleep complaints other than SRBD. Exclusion of obese subjects was due to evidence of a correlation between body mass index and depression in children.[28] The control group consisted of 107 healthy children (43 males and 64 females, mean age 10.2 ± 2.44 years) enrolled in schools within the Campania region. All subjects were recruited from the same urban area, and were of Caucasian origin and middle socioeconomic status. Informed consent was obtained from all parents. The investigation was carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000. The departmental ethics committee of the Second University of Naples approved the study (protocol number 003/2011).

## Sleep evaluation

In all children (with or without SRBD) a cardiorespiratory device (Embletta X10; Embletta PDS, MedCare Flaga, Iceland) was used to perform an overnight respiratory evaluation. The Embletta device is used specifically to detect the presence of SRBD and to assess its severity, is suitable for use both in a sleep laboratory and at home,[29] and has been validated against full polysomnography.[30] All evaluations were performed overnight in the sleep laboratory at the Sleep Center for Developmental Age of Child and Adolescent Neuropsychiatry, Department of Second University of Naples. All recordings started at the subjects' usual bedtime and continued until spontaneous morning awakening.

The parameters measured were: nasal airflow, using two appropriately placed thermistors; thoracoabdominal movements via two piezoelectric bands; pulse oximetry using a finger probe; snoring episodes detected via a vibration sensor placed anterior to the sternocleidomastoid muscle; and continuous actigraphy to monitor and record body position. Recordings were analyzed manually using the device-specific software (Somnologica for Embletta 3.3; Embla, Broomfield, CO). Sleep onset was estimated as the beginning of the first 10-minute period not containing any changes in body position and morning awakening as the end of the last such 10-minute period.[31] Estimated sleep time was calculated as the time between sleep onset and morning awakening. Recordings were analyzed for artefactual or uninterpretable periods of nasal flow, thoracic effort, abdominal effort, or oximetry. Movement periods and artefactual or uninterpretable periods were excluded from the estimated sleep time if they lasted for more than 5 minutes, and the corrected estimated sleep time was calculated.[31] A minimum of 5 hours of corrected estimated sleep time was required.

All the recordings were visually scored by one of the investigators (MC) according to pediatric criteria.[32–35] Specifically, obstructive apnea was defined as cessation

of airflow, lasting for at least two breaths, in the presence of paradoxical ribcage and abdominal movements. The hypopnea index was defined as a reduction in the nasal flow curve signal by more than 50% that was accompanied by either oxygen desaturation or arousal. Central apnea was defined as the absence of airflow at both the nose and mouth with absent inspiratory effort throughout the duration of the event, lasting 20 seconds or longer, or two missed breaths accompanied by at least a 3% oxygen desaturation, an arousal, or an awakening. The apnea-hypopnea index (AHI) was defined as the number of obstructive apneas and hypopneas per hour of sleep,[32,33,36] and the lowest oxygen saturation value and number of desaturation events by 4% and to 90% were counted. The oxygen desaturation index (ODI), defined as events per hour, was also calculated. An AHI and ODI $\leq$ 1 per hour were considered to be normal according to American Thoracic Society criteria.[32,33]

## Screening for depressive symptoms

All children filled out the Italian version of the Children Depression Inventory (CDI)[37] to screen for the presence of depressive symptoms. The CDI is a self-rating scale widely used to assess depressive symptomatology in children and adolescents aged 8–17 years (Cronbach's $\alpha$ = 0.80). It is comprised of 27 Likert-like items, with scores ranging from 0 to 2, and yields total scores from 0 to 54, with higher scores reflecting greater symptomatology. According to Italian validation criteria, a score of 19 is considered suggestive of depressive symptoms.[38] In our study, the five CDI subscales (negative mood, interpersonal problems, ineffectiveness, anhedonia, negative self-esteem)[39,40] were not considered because of lack of normative data for the Italian version of the test.[38]

## Statistical analysis

A *t*-test was performed in order to determine if there were any differences in age, AHI, ODI, and CDI values between the two groups. The Chi-square test was used to describe the sex distribution. The Pearson's correlation test was computed to analyze the relationship among CDI scores with respiratory indices (AHI and ODI). A logistic regression was generated to estimate the odds ratio, respectively, of AHI $\geq$ 3 and ODI $\geq$ 1 being associated with depressive symptoms. *P* values $<$ 0.05 were considered to be statistically significant. Bonferroni correction was applied. All data were coded and analyzed using the commercially available Statistica 6.0 package for Windows (StatSoft Inc, Tulsa, OK). Receiver-operating characteristic curve analysis was calculated using MedCalc software version 7.3.0.1 (MedCalc Software, Mariakerke, Belgium) in order to evaluate the cutoff points for AHI and ODI that could cause depressive symptoms.

# Results

The two groups did not differ in sex (Chi-square 2.414; $P = 0.12$), age ($P = 0.52$), or body mass index ($P = 0.649$) distribution, as shown in Table 1. The group with SRBD had higher mean CDI scores and a rate of pathological CDI scores ($\geq$19) than the control group, as reported in Table 1. The Pearson's correlation test, computed for the whole study population, showed a positive correlation between CDI score and AHI (r = 0.4246; $P < 0.001$) and ODI (r = 0.4393; $P < 0.001$) values. Logistic regression showed that both AHI $\geq$ 3 (odds ratio 3.0565; 95% confidence interval [CI]: 1.6758–5.5746) and ODI $\geq$ 1 (odds ratio 3.0727; 95% CI: 1.6727–5.6445) could be considered risk factors for the development of depressive symptoms.

Receiver-operating characteristic curve analysis showed that the cutoff point for AHI values that could cause a pathological CDI score (ie, $\geq$19) was $>$5.66 (95% CI: 0.680–0.805), with a sensitivity of 61.4 (95% CI: 49–72.8) and a specificity of 88.5 (95% CI: 81.7–93.4). Moreover, a pathological CDI score could be caused by an ODI cutoff point $>$ 4.2 (95% CI: 0.58–0.720), with a sensitivity of 38.6 (95% CI: 27.2–51) and a specificity of 91.5 (95% CI: 85.4–95.7).

# Discussion

In 1976, Guilleminault et al first identified the pediatric form of obstructive sleep apnea, and since then SRBD has become increasingly recognized as a specific entity in childhood.[41,42] Further, depression seems to be the most common mood disorder associated with obstructive sleep apnea syndrome,[22–25] although not all studies have found a

**Table 1** Demographic and clinical characteristics of the study population

| | SRBD (n = 94) | Control (n = 107) | *P* value* |
|---|---|---|---|
| Age | 10.15 ± 2.60 | 10.20 ± 2.44 | NS |
| Sex M/F | 49/45 | 43/64 | NS |
| BMI | 18.93 ± 1.47 | 19.02 ± 1.33 | NS |
| AHI | 8.26 ± 5.77 | 0.95 ± 0.24 | <0.001 |
| ODI | 3.82 ± 3.65 | 0.30 ± 0.28 | <0.001 |
| CDI (mean values) | 21.94 ± 8.07 | 17.59 ± 3.87 | <0.001 |
| CDI (≥19) | 50/44 | 24/83 | <0.001 |

**Note:** *P, Bonferroni-corrected value.
**Abbreviations:** BMI, body mass index; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; CDI, Child Depression Inventory; NS, not statistically significant; SRBD, sleep-related breathing disorder.

clear correlation.[22–24,43] However, studies of the relationship between depressive symptoms and obstructive sleep apnea syndrome in adult subjects have had conflicting findings,[17,44,45] although depression seems to be not uncommon in patients with obstructive sleep apnea.[46] A putative link between depression and obstructive sleep apnea syndrome could be explained by magnetic resonance maps showing damage in the bilateral hippocampus and caudate nuclei, anterior corpus callosum, right anterior thalamus, and medial pons.[47]

Individuals with severe generic sleep problems are more likely to have emotional, school attendance, hyperactivity, and behavioral difficulties[48] than those with no or mild sleep complaints. Moreover, patients with SRBD showed a high rate of internalizing problems (such as anxiety and depression),[49] as confirmed by our results that showed a higher rate of depressive symptoms in children with SRBD than children without SRBD.

On the other hand, sleep problems are a consistent and preventable etiological cause of depressive symptoms, and the correlation between clinical depressive symptoms and AHI ($r = 0.4246$; $P < 0.001$) and ODI ($r = 0.4393$; $P < 0.001$) in our study may be interpreted according to this point of view.

In fact, respiratory problems during sleep should not be considered a minor problem in childhood, given a report of a specific neurocognitive phenotype of pediatric obstructive sleep apnea that may reflect a dysfunction in the prefrontal cortex.[50] In 2010, Torelli et al[51] showed a specific alteration in hippocampal volume in adults affected by obstructive sleep apnea syndrome, indicating abnormality in the limbic areas[52] which are involved also in the pathophysiology of depression,[53] as confirmed in a recent report by Canessa et al using a combination of neuropsychologic testing and voxel-based morphometry.[54] Our results also suggest that an AHI $\geq 3$ and an ODI $\geq 1$ can be considered consistent risk factors for development of depressive symptoms (odds ratios 3.0565 and 3.0727, respectively). Therefore, the modality used to identify sleep-disordered breathing in children affected by mood disorders is clearly important. Alternatively, we should take into account some limitations of this study, ie, our data are derived from a one single psychometric test and not from a complete psychiatric evaluation, and our subjects came from a small group from Southern Italy. Our findings suggest a key role of mood assessment in children affected by SRBD, given that the latter may exacerbate the tendency to develop depressive symptoms, and also because treatment of SRBD could improve or possibly prevent depressive symptoms.[55]

## Disclosure

The authors report no conflicts of interest in this work.

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