

## **Nocturnal obstructive respiratory events severity is associated with low parental quality.**

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### **Abstract**

**Objective:** Despite of the large prevalence of obstructive sleep apnea syndrome (OSAS) in pediatric age, numerous aspects of its impact on day life and on parental quality are still poor studied and considered in the clinical management. The study evaluated the stress levels and coping styles in a large sample of mother of children with OSAS.

**Method:** 374 mothers of children affected by OSAS (mOSAS) were compared with a group of mothers of 421 neurotypical healthy children (mTDC) for stress perceived stress levels and for coping strategies. Subjects were recruited from Italian Regions in Sicily, Campania, Calabria and Umbria.

**Results:** Among both groups mOSAS and mTDC no differences were reported for children age ( $p=0.340$ ), children gender ( $p=0.956$ ), similarly for age of mothers ( $p=0.188$ ).

**Discussion:** The perceived stress assessment in mOSAS showed higher rate of all parental stress scores of PSI-SF: Parental Distress domain ( $p<0.001$ ), Difficult Child subscale ( $p<0.001$ ), Parent-Child Dysfunctional Interaction domain ( $p<0.001$ ) and Total Stress subscale score ( $p<0.001$ ) than mTDC. Regarding the CISS evaluation, mOSAS reported higher scores in emotion-oriented ( $p<0.001$ ) and avoidance-oriented ( $p<0.001$ ) scales, while low task-oriented coping style scale score was reported ( $p<0.001$ ) than mTDC. Pearson's correlation analysis showed significant values for AHI, ODI and mdes SpO<sub>2</sub> for each scale of PSI-SF questionnaire, particularly relevant for P-CDI ( $p<0.001$ ), DC ( $p<0.001$ ) and Stress Tot ( $p<0.001$ ).

**Conclusion:** Pediatric OSAS tends to cause maternal high stress levels than controls, with a significant correlation between respiratory parameters and all PSI-SF scores. Moreover, mothers of affected children showed significantly differences in emotion-oriented and avoidance-oriented coping tasks. The present study suggested the importance of evaluation for caregivers of children affected by OSAS.

**Keywords:** Caregiver stress, Nocturnal respiratory troubles, Coping strategies.

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## Introduction

Among nocturnal respiratory troubles, the obstructive sleep apnea syndrome (OSAS) is the most relevant consisting in upper airway obstruction with intermittent hypoxia disrupting the normal nocturnal ventilation patterns and sleep macrostructure [1].

OSAS may affect pediatric age, with the highest incidence among 2-6 years [2], and general prevalence ranging from 1.2 to 5.7% [1]. Many and different comorbidities are recognized as direct effect of OSAS among affected children, particularly for daytime and executive functioning, metabolic, behavioural and mood regulation [3-7], suggesting an intrinsic complexity for OSAS etiology and clinical aspects in pediatric age respect of adulthood. In general, the quality of life of subjects affected by OSAS seems to be considerably altered also in pediatric age as remarked by many reports [8], although with no correlation with polysomnographic (PSG) data [9].

Moreover, OSAS effects on parenting styles are still scarcely studied and undervalued, despite of the evidence of relevant clinical impact, considering how badly perceived a chronic condition such as OSAS in parents could be the difference between good compliance with treatment and therapeutic failure. In daily clinical practice it is appropriate to consider and emphasize that pediatric OSAS cases are often mild and are intercepted by the clinician for other reasons not related to sleep such as attention difficulties or learning problems. Less frequently the child is taken to a medical consultation due to the presence or persistence of nocturnal enuresis. In this perspective, it is relevant how the communication of the diagnosis of OSAS causes, especially in mothers, a situation of alarm and feelings of fear for the health of the baby that were previously absent. Then, a sort of catastrophization appears on the outcome of this pathology and this greatly influences the perception of your child, first considered healthy and then ill in serious danger of life.

Clearly, this perception may be considered as appropriate only for those cases of pediatric OSAS linked to severe obesity, already associated with metabolic syndrome. For mild or even moderate cases, this perception is certainly not consonant with the reality of the facts.

On the other hand, in pediatric subjects the parental reports about nocturnal respiratory habits cannot be considered reliable properly, because of relevant differences between PSG laboratory and questionnaire recorded data respect of other specific respiratory chronic diseases [10,11]. Overall, nocturnal respiratory symptoms have a significant impact on general familial health with possible reduction also in caregivers' quality style [12-14] probably due to the specific low locus of control and in memory performances as reported in 2019 by Smirni et al. [15]. To the best of our knowledge, studies about the impact of OSAS on parenting are still scarce and therefore the study hypothesis was the impairment of maternal copying styles in a sample of children with OSAS diagnosed by nocturnal cardiorespiratory monitoring.

## Materials and Methods

### Study design

The study design was carried as case control study in the University Sleep Lab for Developmental Age in Sicily, Campania, Calabria and Umbria Italian Regions. All patients were recruited from January 2011 to November 2016.

We selected the mothers of children identified by PSG as affected by OSAS (mOSAS) compared with mothers of neurotypical children (mTDC) in order to proceed to the perceived stress levels and coping strategies assessment.

### Ethics statement

The protocol study was approved by Clinical Departmental University Ethics Committee at University of Palermo and retrospectively registered (EudraCT number n° 2015-001160-19). Study was conducted according to the Declaration of Helsinki criteria [16]. All parents of both groups of children approved the study participation with written consent and similarly mothers accepted to participate to the present study.

### Inclusion and exclusion criteria

Children of both sexes were included if the polysomnographic evaluation (PSG) identified OSAS of any severity.

Exclusion criteria were allergies; neurological and psychiatric disorders, cognitive problems; overweight and obesity and psychoactive drug administration.

### Study population

374 mothers of children affected by OSAS (mOSAS) (268 boys, 106 girls, mean age  $8.61 \pm 1.97$ ; ranging from 6 to 11 years) were compared with a group of mothers of 421 neurotypical healthy children (mTDC) (302 boys, 119 girls; mean age  $8.74 \pm 1.85$  years) were recruited from Italian Regions in Sicily, Campania, Calabria and Umbria. Children of both groups were similar for socioeconomic status and similar for age and gender within the groups: OSAS were 268 boys, 106 girls, mean age  $8.61 \pm 1.97$  vs. TDC 302 boys, 119 girls; mean age  $8.74 \pm 1.85$  years.

### Sleep evaluation

An overnight polysomnography was performed and we took into account only nocturnal respiratory events [17,18]. Both children groups were evaluated in pediatric sleep laboratory. Respiratory parameters (central, obstructive and hypopnea events) were measured and visually scored by an experienced investigator (MC) according to the international pediatric criteria [19,20], with a minimum recording duration  $\geq 300$  minutes.

The apnea/hypopnea index (AHI) was identified as number of respiratory events per sleep hour and mean oxygen saturation ( $SpO_2$ ),  $SpO_2$  nadir were also determined if more than 3% decrease in the  $SpO_2$  level [19]. Moreover, the oxygen desaturation index (ODI) was computed as number of desaturation events per hour of sleep [19-21].

According to the obstructive apnea/hypopnea index (AHI) on PSG, OSAS were defined as mild, moderate or severe if AHI was >1 to <5, ≥ 5 to <10, and ≥ 10 [20,21].

**Parenting Stress Index-Short Form (PSI-SF)**

The Italian official version of the Parenting Stress Index Short Form test (PSI-SF) was used in order to assess the referred maternal stress levels in mothers of children with OSAS and among the control group [22-24]. The PSI-SF is 36 items Likert-like scale (from 0 to 5 points) with high internal consistency (Cronbach s alpha 0.92). The questionnaire consists of four areas: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), Difficult Child (DC) and Total Stress (Stress Tot) domains. The pathological score corresponds to 75 pc with higher values corresponding to high stress levels. In this study, the PSI-SF was administered only to the mother, being the parent assumed to usually spend more time with the children [23-25].

**Coping Inventory for Stressful Situations (CISS)**

In order to evaluate the coping strategies in mothers of children among the both groups, the Italian version of Coping Inventory for Stressful Situations (CISS) was used [26,27]. This self-report test describes the cognitive styles and behavioral resources against specific stressor [26], evaluating three coping strategies: task-oriented, emotion-oriented, and avoidance-oriented. CISS is a Likert-like scale points ranging from 1 to 5 [26,28].

**Statistical analysis**

The independent samples t-test was applied to compare the two groups for age, nocturnal respiratory parameters, PSI-SF and the CISS and chi-square test was applied for gender comparison. In order to analyze the relationship between respiratory parameters and PSI-SF results in OSAS children, Pearsons correlation was applied. p-values ≤ 0.05 were considered as statistically significant. The STATISTICA software (v 6.0; StatSoft Inc, Tulsa, OK, USA) was used to perform all the described analysis.

**Results**

Among both groups mOSAS and mTDC no differences were reported for children age (p=0.340), children gender (p=0.956), similarly for age of mothers (36.4 ± 5.8 vs. 35.9 ± 4.9; t=1.317; p=0.188).

The perceived stress assessment in mOSAS showed higher rate of all parental stress scores of PSI-SF: Parental Distress domain (27.78 ± 9.18 vs. 25.92 ± 4.13; p<0.001), Difficult Child subscale (32.46 ± 9.79 vs. 22.66 ± 2.17; p<0.001), Parent-Child Dysfunctional Interaction domain (23.89 ± 8.99 vs. 20.16 ± 2.96; p<0.001) and Total Stress subscale score (84.14 ± 24.89 vs. 62.73 ± 14.39; p <0.001) than mTDC (Table 1).

Differently, Defensive Responding domain scores were similar between the two groups (17.25 ± 5.57 vs. 16.93 ± 5.89; p=0.439) (Table 1).

Regarding the CISS evaluation, mOSAS reported a high scores in emotion-oriented (65.17 ± 9.74 vs. 45.01 ± 10.93; p<0.001) and avoidance-oriented (61.75 ± 10.19 vs. 42.89 ± 11.02; p <0.001) scales, while low task-oriented coping style scale score was reported (12.25 ± 9.97 vs. 55.86 ± 10.09; p<0.001) respect of than controls’ mothers (Table 2).

**Table 1.** Shows the differences in mothers of children affected by Obstructive Sleep Apnoea Syndrome (mOSAS) and mothers of typical developing children (mTDC) for Parenting Stress Index—Short Form (PSI-SF) scales: PD (parental distress);PCDI (parent-children dysfunctional interaction); DC (difficult child); DEF (defensive responding). According to the t-Test analysis. p values 0.05 were significant.

Variables	mOSAS n=374	mTDC n=421	p
PD	27.78 ± 9.18	25.92 ± 4.13	0.001
PCDI	23.89 ± 8.99	20.16 ± 2.96	0.001
DC	32.46 ± 9.79	22.66 ± 2.17	0.001
DEF	17.25 ± 5.57	16.93 ± 5.89	0.439
Total Stress	84.14 ± 24.89	62.73 ± 14.39	0.001

**Table 2.** Shows the differences in mothers of children affected by Obstructive Sleep Apnoea Syndrome (mOSAS) and mothers of typical developing children (mTDC) for Coping Inventory for Stressful Situations (CISS) test scores, according to the t-Student’s analysis. p values <0.05 were considered statistically significant.

Variables	mOSAS n=374	mTDC n=421	p
Task-oriented	12.25 ± 9.97	55.86 ± 10.09	0.001
Emotion-oriented	65.17 ± 9.74	45.01 ± 10.93	0.001
Avoidance-oriented	61.75 ± 10.19	42.89 ± 11.02	0.001

As reported in Table 3, the Pearson’s correlation analysis showed significant values for AHI, ODI and mdes SpO<sub>2</sub> for each scale of PSI-SF questionnaire, particularly relevant for P-CDI (r= 0.6678; p<0.001), DC (r=0.6602; p<0.001) and Stress Tot (r= 0.6853; p<0.001).

**Discussion**

OSAS may be considered as too complex clinical condition to be confined to nighttime respiratory disease only. Clinical evidence points out that OSAS is a condition with high impact on all aspects of the life of affected children, including those related to parental quality. In this perspective, our findings reported in mOSAS higher stress general levels respect of mothers of controls (84.14 ± 24.89 vs. 62.73 ± 14.39; p 0.001), particularly for Parental Distress (27.78 ± 9.18 vs. 25.92 ± 4.13; p<0.001), Difficult Child (32.46 ± 9.79 vs. 22.66 ± 2.17; p<0.001) and Parent-Child Dysfunctional Interaction subscales (23.89 ± 8.99 vs 20.16 ± 2.96; p=0.001), pinpointing the impaired perception of their own not healthy children.

The basic idea of this study is similar to that already published by Smirni et al. in 2019 which highlighted high levels of stress in a sample of mothers of children with OSAS, also specifying

peculiar neuropsychological difficulties. The difference of the present study is evaluating a larger sample (795 mothers in

total), coping strategies in addition to the perceived parental stress levels.

**Table 3.** According to the Pearson's analysis was reported the correlation relationship between sleep respiratory parameters (Apnea/hypopnea index, AHI; Oxygen desaturation index, ODI; Mean Oxygen saturation, mSpO<sub>2</sub>; Nadir of Oxygen saturation, nSpO<sub>2</sub>; Mean Oxygen desaturation, mdes SpO<sub>2</sub>) of children affected by Obstructive Sleep Apnoea Syndrome (OSAS) and Parenting Stress Index—Short Form (PSI-SF) scales: PD (parental distress); PCDI (parent-children dysfunctional interaction); DC (difficult child); DEF (defensive responding) of their mothers. *p* values < 0.05 was considered significant.

Variables	PD	P-CDI	DC	DEF	Stress Tot
AHI	r=0.4994; p<0.001	r=0.6678; p<0.001	r=0.6602; p<0.001	r=0.4254; p<0.001	r=0.6853; p<0.001
ODI	r=0.3326; p<0.001	r=0.4839; p<0.001	r=0.4366; p<0.001	r=0.2851; <0.001	r=0.4691; p<0.001
mSpO <sub>2</sub>	r=0.0300; p=0.563	r=0.0840; p=0.105	r=0.0793; p=0.126	r=0.0059; p=0.910	r=0.0726; p=.161
nSpO <sub>2</sub>	r=-0.345; p=0.505	r=0.0319; p=.539	r=-.0608; p=.241	r=-.0543; p=.295	r=-0.0251; p=.628
Mdes SpO <sub>2</sub>	r=0.1802; p<0.001	r=0.2017; p<0.001	r=0.1803; p<0.001	r=0.1846; p<0.001	r=0.2104; p<0.001

In addition, as an element of novelty, these findings for the first time suggested a linearly relationship of total stress level to the AHI severity, ODI and mdes SpO<sub>2</sub> for each scale of PSI-SF questionnaire, particularly relevant for P-CDI (r=0.6678; p<0.001), DC (r=0.6602; p<0.001) and Stress Tot (r=0.6853; p<0.001).

We could speculate that parents may be worried for the health of their own children when OSAS symptoms and signs become significant and disturbing for nocturnal sleeping, fearing for the an apparent life threatening events (i.e. apnoeic events with moaning and/or gasping). On the other hand, when nocturnal respiratory events are evident for caregivers, also diurnal OSAS signs may be surely most disturbing such as motor hyperactivity, inattention, mood disorders, excessive daytime sleepiness [5-7].

Moreover, OSAS symptoms tend to establish slowly and chronically, impacting on different neuropsychological skills [29] with consequent parents' worrying related and dependent to their coping strategies.

Specifically, mOSAS seems to present an higher rate of emotion-oriented (65.17 ± 9.74 vs. 45.01 ± 10.93; p<0.001) and avoidance-oriented (61.75 ± 10.19 vs. 42.89 ± 11.02; p<0.001) coping styles that include an higher rate of self-oriented reactions including emotional responses, self-preoccupation, and fantasizing, or the presence of activities and cognitive changes aimed at avoiding the stressful situation by distracting oneself with other situations or tasks, or via social diversion as a means of alleviating stress, than mother of healthy children (p < 0.001).

Conversely, mOSAS show lower rate of task-oriented coping strategies (12.25 ± 9.97 vs. 55.86 ± 10.09; p<0.001) highlighting a sort of paucity in emotional and cognitive skills related to the ability to face the pathological situation of their children in a fair and real way. These findings suggest that the improvement in parental stress management of mOSAS may be part of the therapeutic program shared with children affected starting from the OSAS severity.

We have taken into account as main study limitation the lack of therapeutic follow-up in the middle or long term, considering

that the present research was only focused on identifying possible alteration coping strategies in mOSAS. This study represents an important starting point for further studies aimed at verifying the impact and effect of psychotherapy aimed at dysfunctional maternal aspects, aimed at verifying the possible improvement of therapeutic compliance. However, this study was configured as a pilot exploratory investigation to identify problematic parenting aspects in children with OSAS compared to parents of healthy children.

## Conclusion

In conclusion, our study tends to highlight a new aspect of a pathology still underestimated in its multiple aspects in the pediatric age. Our results suggested a new aspect to consider in the management of the pathology, highlighting the importance of evaluation for caregivers for adequate clinical management and in order to improve family compliance.

## References

1. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics* 2012; 130: 576–84.
2. EO, Vgontzas AN, Lin HM, Liao D, et al. Sleep disordered breathing in children in a general population sample: prevalence and risk factors. *Sleep* 2009; 32: 731–736.
3. Brunetti L, Francavilla R, Scicchitano P, et al. Impact of sleep respiratory disorders on endothelial function in children. *Scientific World Journal* 2013; 26: 719456.
4. Esposito M, Antinolfi L, Gallai B, et al. Executive dysfunction in children affected by obstructive sleep apnea syndrome: an observational study. *Neuropsychiatr Dis Treat* 2013; 9: 1087-94.
5. Carotenuto M, Esposito M, Parisi L, et al. Depressive symptoms and childhood sleep apnea syndrome. *Neuropsychiatr Dis Treat* 2012; 8: 369-73.
6. Jackman AR, Biggs SN, Walter LM, et al. Sleep-disordered breathing in preschool children is associated with

- behavioral, but not cognitive, impairments. *Sleep Med* 2012; 13: 621-31.
7. Landau YE, Bar-Yishay O, Greenberg-Dotan S, et al. Impaired behavioral and neurocognitive function in preschool children with obstructive sleep apnea. *Pediatr Pulmonol* 2012; 47: 180-8.
  8. Gomes Ade M, Santos OM, Pimentel K, et al. Quality of life in children with sleep-disordered breathing. *Braz J Otorhinolaryngol* 2012; 78: 12-21.
  9. Baldassari CM, Alam L, Vigilar M, et al. Correlation between REM AHI and quality-of-life scores in children with sleep-disordered breathing. *Otolaryngol Head Neck Surg* 2014; 151: 687-91.
  10. Rosen D. Many parents report their child's breathing and sleep patterns during overnight sleep study as atypical. *Clin Pediatr (Phila)* 2010; 49: 764-7.
  11. Santamaria F, Esposito M, Montella S, et al. Sleep disordered breathing and airway disease in primary ciliary dyskinesia. *Respirology* 2014; 19: 570-5.
  12. McManus IC, Mitchison HM, Chung EM, et al. Primary ciliary dyskinesia (Siewert's/Kartagener's syndrome): respiratory symptoms and psycho-social impact. *BMC Pulm Med* 2003; 3:4.
  13. Glasscoe CA, Quittner AL. Psychological interventions for people with cystic fibrosis and their families. *Cochrane Database Syst Rev* 2008; 16: CD003148.
  14. Eddy ME, Carter BD, Kronenberger WG, et al. Parent relationships and compliance in cystic fibrosis. *J Pediatr Health Care* 1998; 12:196-202.
  15. Smirni D, Carotenuto M, Precenzano F, et al. Memory performances and personality traits in mothers of children with obstructive sleep apnea syndrome. *Psychol Res Behav Manag* 2019; 12:481-487.
  16. World Medical Association World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 27: 2191-4.
  17. Roccella M, Marotta R, Operto FF, et al. NREM Sleep Instability in Pediatric Migraine without Aura. *Front Neurol* 2019;10: 932.
  18. Carotenuto M, Roccella M, Pisani F, et al. Polysomnographic Findings in Fragile X Syndrome Children with EEG Abnormalities. *Behav Neurol* 2019; 2019: 5202808.
  19. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions Task Force of the American academy of sleep medicine. *J Clin Sleep Med* 2012; 8:597-619.
  20. Goh DY, Galster P, Marcus CL. Sleep architecture and respiratory disturbances in children with obstructive sleep apnea. *Am J Respir Crit Care Med* 2000; 162: 682-6.
  21. Wagner MH, Torrez DM. Interpretation of the polysomnogram in children. *Otolaryngol Clin North Am* 2007; 40:745-59.
  22. Esposito M, Marotta R, Roccella M, et al. Pediatric neurofibromatosis 1 and parental stress: a multicenter study. *Neuropsychiatr Dis Treat* 2014;10: 141-6.
  23. Abidin RR. Parenting Stress Index-Short Form Manual. Los Angeles, CA: Western Psychological Services. 1990.
  24. Abidin RR. Parenting Stress Index, 3rd edn: Professional Manual. Lutz, FL: Psychological Assessment Resources Inc. 1995.
  25. Wysocki T, Huxtable K, Linscheid TR, et al. Adjustment to diabetes mellitus in preschoolers and their mothers. *Diabetes Care* 1989; 12: 524-529.
  26. Iavarone A, Ziello AR, Pastore F, et al. Caregiver burden and coping strategies in caregivers of patients with Alzheimer's disease. *Neuropsychiatr Dis Treat* 2014; 10: 1407-13.
  27. Endler NS, Parker JDA. CISS Coping inventory for stressful situations, Edited for Italian version by Saulo Sirigatti, Cristina Stefanile e Stefano Lera. Giunti OS. 2009.
  28. Endler NS, Parker JD. Multidimensional assessment of coping: a critical evaluation. *J Pers Soc Psychol* 1990; 58: 844-854.
  29. Testa D, Carotenuto M, Precenzano F, et al. Evaluation of neurocognitive abilities in children affected by Obstructive Sleep Apnea syndrome before and after adenotonsillectomy. *Acta Otorhinolaryngol Ital* 2020; 40: 1-11.

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