

## ADHD-LIKE SYMPTOMS IN CHILDREN AFFECTED BY OBSTRUCTIVE SLEEP APNEA SYNDROME: A CASE-CONTROL STUDY

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### ABSTRACT

**Introduction:** ADHD is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms. Sleep disorders may be considered as a not secondary underlying cause of ADHD and growing evidence evidenced that obstructive sleep apnea syndrome (OSA) symptoms may overlap ADHD's ones.

*Aim of the present study is verifying the presence of ADHD-like symptoms in other frequent condition such as sleep-related breathing disorders in pediatric age.*

**Materials and methods:** 34 children (19 males and 15 females) aged 6-10 years (mean age  $9.706 \pm 3.434$ ) with polysomnographic diagnosis of OSA, according to ICSD-3 criteria, were recruited. Control group was composed by 89 typical developing children (47 males, 42 females) (mean age  $9.528 \pm 3.351$ ). The Conners' Rating Scale- Revised (CRS-R) test was administered to mothers to assess their children's behavior.

**Results:** The two groups are comparable for age ( $p = 0.794$ ) and sex distribution ( $p = 0.918$ ). Subjects affected by OSA present higher scores in pathological range in all scales of CRS-R than controls (Table 1).

**Conclusions:** Scientific and clinical evidences tend to stress the similarities between ADHD and OSA effects/comorbidities in pediatric age, suggesting sleep screening as mandatory before starting stimulant drugs treatment.

**Keywords:** ADHD, ADHD-like symptoms, obstructive sleep apnea syndrome, OSA.

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### Introduction

In developmental age, the syndrome named as Attention Deficit Hyperactivity Disorder (ADHD) is characterized by inattention, hyperactivity, impulsivity, or a combination of these symptoms, compromising basic everyday functions such as learning abilities, executive functioning, and social skills<sup>(1)</sup>.

Since the first description in 1902 by George Still on Lancet journal, the prevalence studies have

reported different prevalence rates ranging 3% -5% of school-age children, and around 1% in Italian pediatric population<sup>(2)</sup>.

To date, diagnostic criteria are based focus on behavioral symptoms, because the absence of specific biomarkers, although genetic factors, environmental factors, prematurity, low birth weight and hypoxic-ischemic encephalopathy are considered important in ADHD etiology. In this light, the role of sleep disorders may be an interesting and to date not yet well considered as causative factor for

ADHD, despite of many and relevant scientific evidences<sup>(9)</sup>. In fact, sleep disorders may be considered as a not secondary underlying cause of ADHD<sup>(3)</sup>, although still underdiagnosed in pediatric age. On the other hand, there is growing evidence that sleep disorders and mainly the obstructive sleep apnea syndrome (OSA) are associated with behavioral problems and hyperactivity, executive functions impairment, cognitive and learning difficulties<sup>(4-13)</sup>.

Starting from the frequent over-diagnosis among Italian children, the aim of the present study is verifying the presence of ADHD-like symptoms in other frequent condition such as sleep-related breathing disorders in pediatric age.

## Material and methods

34 children (19 males and 15 females) aged 6-10 years (mean age  $9.706 \pm 3.434$ ) with polysomnographic diagnosis of OSA, according to ICSD-3 criteria (14), were recruited.

Exclusion criteria were the following: overweight, obesity, cognitive disability (IQ <70), borderline intellectual functioning, neurological and psychiatric disorders (15-17), chromosomal defects, specific neuropsychological disorder, epilepsy<sup>(18-31)</sup>.

Control group was composed by 89 typical developing children (47 males, 42 females) (mean age  $9,528 \pm 3,351$ ).

All subjects of both groups were recruited within the same urban area, all were Caucasian and homogeneous for socioeconomic status

Ethical approval from the local Research Ethics Center and informed parental consent were obtained.

### *Polysomnographic (PSG) Data*

After reviewing and analyzing PSG data collected from inpatients children between January and June 2016 to establish the presence of OSA in the experimental group, OSA severity was determined according to the current guidelines specified by the American Academy of Sleep Medicine (AASM)<sup>(32)</sup>: mild OSA was defined by an obstructive apnea-hypopnea index (o AHI) of 1 to <5 events per hour; moderate OSA was defined as was defined as  $\geq 5$  to <10 events/hour, and severe OSA  $\geq 10$  events/hour.

### *Conners' Rating Scale-Revised (CRS-R)*

At the clinic visit, Conners' Rating Scale-Revised (CRS-R) was administered to mothers to

assess their children's behavior. CRS-R examines seven types of behavior problems in children including: Oppositional, Anxious-Shy, Cognitive Problem/Inattention, Hyperactivity, Perfectionism, Psychosomatic, and Social Problems. It also contains four index scores: Conners' ADHD Index; Conners' Global Index (CGI): Restless-Impulsive; CGI: Emotional Lability; and CGI: Total. CRS-R also includes scales for the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition<sup>(33)</sup> diagnosis of ADHD:

- a) DSM-IV: Inattentive,
- b) DSM-IV: Hyperactive-Impulsive,
- c) DSM IV: Total.

Higher scores indicate an increased likelihood that a child would meet diagnostic criteria for ADHD. A T-score of 65 indicates a "clinically significant problem"<sup>(34)</sup>.

### *Statistical analysis*

For comparison between the two groups (OSAS and controls) it was applied t- testing and Chi-square test, where appropriate. P values <0.05 were considered statistically significant.

For statistical analysis it used the software STATISTICA (data analysis software system, version 6, StatSoft, Inc. (2001). For the comparison between the groups the t-test was applied. P values <0.05 were considered statistically significant.

## Results

The two groups are comparable for age ( $p = 0.794$ ) and sex distribution ( $p = 0.918$ ). Subjects affected by OSA present higher scores in pathological range than controls in the following domains: hyperactivity, ADHD Index, Restlessness-impulsivity (CGI II), emotional instability (CGI IE), Hyperactivity and other problem areas (CGI T), DSM-IV inattention, DSM -IV hyperactivity and impulsivity, total DSM-IV ADHD, No. Inattention symptoms of DSM-IV, no symptoms of hyperactivity / impulsivity DSM-IV ( $p < 0.001$  for all subscales) (Table 1).

## Discussion

Several studies have focused on alterations of executive functioning in children with OSA, with a putative specific relationship with the degree of respiratory troubles, supporting the role of intermittent hypoxia impact the fronto-prefrontal regions<sup>(6,7,10,35)</sup>.

Considering the more relevant and frequency of OSA respect of ADHD (27% vs. 3-5%) in pediatric age, it is obvious and intuitive that hyperactive school-aged children may be affected by OSA more probable than ADHD.

	OSA N=34	Controls N=89	P
Oppositional	51.02±8.14	49.96±9.03	0.551
Cognitive Problem/Inattention	45.13±6.12	43.01±8.05	0.168
Hyperactivity	71.31±4.18	44.15±6.34	<0.001
Anxious-Shy	40.73±2.17	39.96±2.83	0.155
Perfectionism	46.93±9.15	44.18±8.93	0.132
Social Problems	50.37±7.39	50.93±7.25	0.704
Psychosomatic Problems	50.15±5.03	49.82±5.44	0.759
Conners' ADHD Index	77.36±10.04	45.26±6.19	<0.001
Restless-Impulsive (CGI I-I)	71.86±9.93	44.64±5.61	<0.001
Emotional Lability (CGI I-E)	59.05±6.94	45.11±7.09	<0.001
Hyperactivity and other problems (CGI T)	70.48±9.81	44.25±6.33	<0.001
DSM-IV Inattention	70.66±8.96	49.29±5.90	<0.001
DSM-IV Hyperactivity	75.71±8.83	49.63±4.31	<0.001
DSM-IV ADHD Total score	75.04±10.25	48.06±6.38	<0.001

**Table 1:** Shows differences between children affected by obstructive sleep apnea syndrome (OSA) and typical developing subjects among Conners Rating Scales-Revised version (CRS-R) scales. For comparison between the two groups (OSAS and controls) it was applied t- testing and Chi-square test, where appropriate. *P* values<0.05 were considered statistically significant.

In general, hyperactivity presents higher prevalence as non-specific symptom in several nosographic paintings of childhood neuropsychiatric interest, as a result of a reduction in inhibitory control both motor and behavioral skills. In fact, hyperactive and inattentive behavior has been reported in children with OSA and habitual snoring. In addition, children with higher indices of snoring tend to show lower scores to cognitive and neuropsychological standardized tests. On the other hand, in 2011 a systematic review has shown that the prevalence of OSA in ADHD subjects (25-30%) is higher than that of the general population (about 3%)<sup>(36)</sup>. In this perspective, the present study has as preliminary investigation in the evaluation of hyperactive behavior in school-aged children with OSAS.

Conversely, sleepy children tend to use a greater motor activity pattern to be more vigilant, supporting the parents' report about that when they are very tired appear angry and become aggressive and hyperactive. In this light, the use of stimulant drugs increase the catecholamines activity in the CNS, improving arousal and alertness in typical developing children, identifying it as the best treatment in ADHD to limit motor hyperactivity<sup>(27-29)</sup>.

Moreover, the hypothesis that OSA may represent one of the causes of ADHD is supported by AASM guidelines that recommend screening for sleep apnea among children undergoing evaluation for ADHD<sup>(40)</sup>, because of the overlapping cognitive, neuropsychological and behavioral symptoms and OSA.

In conclusion, scientific and clinical evidences tend to stress the similarities between ADHD and OSA effects/comorbidities in pediatric age, suggesting sleep screening as mandatory before starting stimulant drugs treatment<sup>(41-50)</sup>.

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