

Clinically Oriented Subtyping of Chronic Insomnia of Childhood

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Objectives To identify different profiles of pediatric insomnia, based on the most frequent clinical presentations (nocturnal awakenings, difficulty in falling asleep, nocturnal restlessness, early morning awakenings).

Study design A structured parent interview was conducted in 338 children (mean age 21.29 months, SD 10.56) referred by pediatricians because of insomnia resistant to behavioral approaches and common drug treatments. The aim was to assess the characteristics of insomnia in children, together with family sleep-related history. A latent class analysis was run to identify profiles of insomnia. ANOVA and the χ^2 test were used to examine differences between profiles.

Results A 3-class model was built by latent class analysis: 17% (n = 58) of children constituted the first class, characterized by difficulties in falling asleep, with restlessness, nocturnal restlessness, and awakenings during the night; the second class, characterized by early morning awakenings, comprised 21% (n = 71) of children; 62% (n = 209) of children fell within the third class because of their high frequency of nocturnal awakenings and difficulties in falling asleep. The first class reported longer sleep latency and the presence of restless legs syndrome and anemia in the family history; depression and/or mood disorders were more frequent in class 2 and allergies and/or food intolerance were more frequent in class 3.

Conclusions Our study suggests the existence of 3 different phenotypes of insomnia in children, based on clinical, personal, and familial data. The identification of these different phenotypes might help to optimize the assessment and treatment of insomnia in young children. (*J Pediatr* 2018;■■■:■■■-■■■).

Over the past decades, several studies have been carried out to understand the link between sleep problems and child development in different areas. Significant associations have been found between childhood sleep problems and socioemotional disturbances, school difficulties, and physical diseases.¹⁻⁶ According to these and other studies, identifying children's sleep problems and their prevalence is important for improved treatment and prevention of negative socioemotional and cognitive outcomes.⁷

Researchers have suggested that the parental perception of an overall sleep problem correlates significantly with nocturnal awakenings and difficulties in falling asleep⁸⁻¹¹ and that the frequency of nighttime awakenings is one of the main factors determining the parent judgment of the quality of child sleep.¹²

The prevalence of pediatric insomnia in children and adolescents has been reported to range from 10% to 50%, with greater percentages in children with neurodevelopmental or psychiatric problems.^{7,13-15} Previous studies have reported a prevalence of pediatric insomnia ranging from 25% to 50% in preschoolers,¹⁶ to 37% in children aged 4-10 years,¹⁷ and up to 40% during adolescence.¹⁸ Different definitions and classifications of pediatric insomnia have been used in research or clinical contexts.¹⁹ In the *International Classification of Sleep Disorders, Third Edition* (ICSD-3),²⁰ pediatric insomnia has been incorporated into a single entity with that of adults, under the term of chronic insomnia disorder.

The ICSD-3 defines chronic insomnia as "a persistent difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep, and results in some form of daytime impairment" and reports in the comments that pediatric insomnia may be described considering the following 3 subtypes:

- 1) *Sleep-Onset Association Type*, which includes children who refuse to sleep because they need a specific object or person to fall asleep or get back to sleep. This subtype of pediatric insomnia is quite common in younger infants and characterized by multiple nocturnal awakenings;
- 2) *Limit-Setting Type*, which occurs when parents lose control of the child's behavior during bedtime or awakenings from sleep. This subtype of pediatric insomnia is often observed in older infants, who tend to oppose their parents, especially during bedtime; and
- 3) *Combined Type*, which is characterized by mixed symptoms of the 2 previous subtypes.

ICSD-3 *International Classification of Sleep Disorders, Third Edition*
LCA Latent class analysis

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The absence of a specific symptom-based classification of insomnia for children may explain the inadequacy of the screening for sleep problems, as well as the underdiagnosis of insomnia in childhood.^{11,21}

This conceptual discussion also has been reported in adults. Subtypes of insomnia have been proposed in the major classification systems; however, a seminal study concluded that the reliability and validity of the different nosological entities included was so poor that they did not improve diagnostic accuracy and that alternate diagnostic paradigms for insomnia classification should be considered.²² As a consequence, the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* and the ICSD-3 abandoned further subtyping of chronic insomnia.^{20,23} Thus, from a clinical point of view, the ICSD-3 generic classification of insomnia might limit the identification of symptomatic subtypes of pediatric insomnia and does not guide specific treatment for the different manifestations of insomnia.⁷

It is largely accepted that various phenotypes exist, but their specific identification is lacking. Recent studies have emphasized the role of genetic factors in the development of insomnia of childhood: heritability contributed to a large extent to specific symptoms such as nocturnal sleep duration and nighttime awakenings,^{24,25} suggesting that a more accurate method of investigating the heritability of insomnia needs to focus on the specific symptoms constituting the disorder separately, rather than relying on an overall “insomnia” construct.²⁶

Based on these considerations, in this study, we sought to describe whether specific sleep complaints and clinical features might represent different pathophysiologic subtypes of insomnia. We aimed to identify different profiles of pediatric insomnia based on the sleep problems reported by parents, patient factors, and sleep-related family history.

Methods

Three hundred thirty-eight children (227 boys) aged 6-48 months (mean = 21.29, SD = 10.56) were consecutively recruited during their first medical visit for “insomnia” at the Pediatric Sleep Center of the Sapienza University, Rome, Italy. Children were referred by pediatricians because of their insomnia resistant to common treatments (mainly over-the-counter products) and not responding to behavioral approaches.

All parents reported that they tried to apply the extinction or graduated extinction, based on instructions found in specific books or the Internet, or that they were guided by the pediatricians without success. Most of the parents affirmed that they found extinction sleep interventions too difficult and stressful to implement for several reasons (eg, enduring crying, practical considerations, fear of possible repercussions, incongruence with individual beliefs, different cultural practices).²⁷

The following exclusion criteria were used: (1) presence of diagnosed medical problems (ie, recurrent otitis, persistent snoring or sleep apnea noted by parents, intercurrent lung or bowel diseases, etc), malformations, or neurologic/psychiatric disorders; and (2) intercurrent diseases that would require treatment with drugs that affect sleep (eg, steroids, antihista-

mines). The study was approved by the Ethics Commission of the Department of Developmental and Social Psychology (Sapienza University of Rome), and parental written consent was obtained for all children.

Interview on Pediatric Insomnia

A semistructured interview was conducted by trained physicians to assess the characteristics of the child’s insomnia, together with the patient’s medical history and family history. The interview contained questions addressing the presence or absence of difficulties in falling asleep, difficulties in falling asleep with restlessness, nocturnal restlessness, multiple night awakenings (≥ 3), and early morning awakening. We chose these variables based on the most frequently reported sleep complaints according to the literature²⁸⁻³² and on the authors’ own clinical experience. These attributes were selected for subsequent latent class analysis (LCA). The parental perception of a sleep problem is mediated by 2 main descriptors: awakenings and difficulties falling asleep⁹; however, other common complaints also are related to nocturnal restlessness, sleep onset, and early morning awakenings.

The semistructured interview also included questions regarding child bedtime, wake-time, and sleep latency. Finally, questions on family history for difficulties potentially related to sleep (eg, depression/mood disorders, anemia, restless legs syndrome) and additional child complaints (eg, colic, allergies, gastroesophageal reflux, anemia) were included. These last questions were coded in terms of presence or absence.

Statistical Analyses

Descriptive analyses were run on the overall sample with SPSS for Windows, Version 18.1 (SPSS Inc, Chicago, Illinois). Then, an LCA by using Mplus 5.1 (Los Angeles, California)³³ was conducted to identify different profiles of pediatric insomnia. LCA was run considering the following sleep dichotomous variables: (1) difficulties in falling asleep, (2) difficulties in falling asleep with restlessness, (3) nocturnal restlessness, (4) early morning awakenings, and (5) multiple night awakenings (≥ 3). All of these variables were coded in terms of presence or absence.

To better identify the best solution of profiles of pediatric insomnia, we ran several models (ranging from 2 to 4 classes). The best model was chosen considering 2 criteria^{34,35}: the Akaike information criterion and the Bayesian information criterion. We chose the best solution based on the smallest Akaike information criterion and Bayesian information criterion. We also considered the entropy index with values close to 1, meaning better homogeneity among groups. Finally, the resulting classes were compared with each other, considering both additional child complaints and family history for sleep problems. Specifically, ANOVAs were run considering differences between classes regarding sleep continuous variables (ie, bedtime, wake-time, and sleep latency). The Bonferroni post-hoc analysis was used to test specific differences among classes. The χ^2 test was used to analyze differences between the classes on dichotomous variables related to the child (eg, allergies, gastroesophageal reflux, and anemia) or family (eg, depression/

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