

Article

Subjective Assessment of Sleep in Infantile Autism, Comparative Study

Maydelin Alfonso Alfonso ^{1,*} Lilia María Morales Chacón ², Justa Elizabeth González Naranjo ³ and Ana Margarita Valiente Linares ⁴

¹ Clinical Neurophysiology of CIREN Havana, Cuba

² Clinical Neurophysiology of CIREN Havana, Cuba; Lily@neuro.ciren.cu

³ Clinical Neurophysiology of CIREN Havana, Cuba; egonzalez@neuro.ciren.cu

⁴ Clinical Neurophysiology of CIREN Havana, Cuba; ana.valiente@nauta.cu

* Correspondence: malfonso@neuro.ciren.cu; Tel.: +53-05-392-12-81

Abstract: Sleep disturbances very common in children with autism. That is why it requires instruments that facilitate its evaluation. Goals: Perform the evaluation of sleep from a subjective prospect in a group of children with primary autism and compare to a control group, using the Sleep Habits in Children Survey (CSHQ), In order to determine sleep disturbances, according to the sub-scales results. Method: A prospective cross-sectional study of the sample was carried out. A group with primary Autism n = 21 was selected. For the assessment of the dream we chose (CSHQ). The differences between independent groups were calculated by applying a Mann Whitney U test (p < 0.05). Results: The group of children with autism showed the highest values of the total scale (mean = 48.00) which is congruent with a greater dysfunction of sleep, compared to the control group (mean = 36.47) for p = 0.00. Significant differences were found for all sub scales p = 0.00, with the exception of sub-scale number 7. Conclusions: There is a high presence of sleep disturbances in children with primary autism, which are related to multifactorial causes, with the exception of sleep breathing disorders that did not show statistically significant differences between groups.

Keywords: Subjective sleep assessment; Autism spectrum disorder; REM sleep; NREM sleep

1. Introduction

Autism is a neurodevelopmental disorder characterized by a deficit in 3 major domains: in social interaction, language development and communication. In these children are very common sleep disturbances.

Sleep is one of the necessary functions for all persons. The sleep in the child follows a development process from the fetal stage, and persist in an especial way during the first years of life. The REM sleep phase is very important too in the first months of live, because it is related to the maturation of the cerebral cortex [1, 2]

With a prevalence of 20-50 cases per 10,000 inhabitants. It is more frequent in males (3: 1) and usually the clinical manifestation starts after the first year of life [3]. Autistic children are generally considered poor sleepers. Between 33 and 44% of children with autism suffer from sleep disorder [4, 5] the onset and maintenance insomnia is the most reported. Moreover, insomnia in autistic children has been found to alter parent's sleep and add tremendous stress to their families' lives [6]. Hypotheses regarding intrinsic causes of insomnia in these children include brain wave organizational and maturational differences, circadian-relevant genes, abnormal melatonin production, and arousal and sensory dysregulation [7].

The altered sleep and the posterior diurnal sleepiness have a negative impact on the behavior of these children which often manifests hyperactivity, lack of attention and aggression [8, 9]. The

neurobiological causes of sleep disturbances in autism are abnormalities in GABA (gamma amino butyric acid), the neurotransmitter involved in promoting sleep and a regular sleep – wake cycle, regarding clock gene anomalies. Different studies report a reduced GABA in these patients [10, 11, 12].

On the other hand, melatonin in blood and urine are decreased in autism, which leads to alterations in the circadian rhythm [13, 14]. Low melatonin and clock gene anomalies in people with autism seem to be involved in social and circadian problems [15]. Melatonin, a hormone synthesized in the pineal gland from serotonin, exhibits a circadian pattern with low daytime concentrations and elevated overnight levels and mainly contributes to the regulation of circadian rhythms [16]. In a small group study, plasma melatonin profiles are comparable to those reported in the literature for typically developing children, and actigraphic sleep onset occurs when plasma melatonin levels rise [17].

Sleep disturbances in individuals with autism can be ascribed to biological, psychological, and social environmental factors [18]. These were the causes that motivated us to carry out this study. We consider it of great value to have an instrument to provide us with data not only about the night's sleep, but also about the diurnal habits and social interaction of these patients. With these data we could complete the evaluation of sleeping of autistic children that we frequently receive in the neurophysiology laboratory in order to complement the objective evaluation regarding sleep disturbances.

In a previous study to this investigation, we conducted a review of the different questionnaires proposed in the literature in order to find an instrument that we could use in our laboratory [19-23]. We chose (CSHQ) since it is a retrospective questionnaire. It evaluates sleep habits in children between 2 and 10 years old collecting data from the previous week, which reduce the risk of error by subjectivity. The questionnaire is an abbreviated version of 33 items includes the symptoms of the most common sleep problems according to the international classification of sleep disturbances grouped into eight sub-scales [23] written in English. In order to make an easier understanding for parents we validated the questionnaire in Spanish and it was adapted to the socio-cultural conditions of Cuban families.

Counting on the benefits of this instrument, we focus our attention on childhood autism, with the goal to perform the evaluation of the sleep from a subjective prospect in a group of children with primary autism and compare it to a control group, using the Sleep Habits in Children Survey (CSHQ), in order to determine sleep disturbances, according to the sub-scales. We found a great presentation of sleep disorders in autistic children in accordance with what is described in the literature.

2. Materials and Methods

A prospective cross-sectional study of the sample was conducted in the period between November 2016 and February 2017.

Previously in 2015 we carried out a validation work on the questionnaire where we obtained results that showed that this instrument had the appropriate psychometric properties to evaluate the sleep habits of Cuban children in the age range of interest, and that in turn was a highly reliable instrument (this work is currently being published in the Cuban pediatric journal).

Healthy controls were recruited in schools and children's centers with a total score of less than 40 points, which corresponds to a higher quality of sleep. The group of autistic children was evaluated by neurologist in other medical centers, and were seen in our laboratory with a confirmed diagnosis of primary Autism [24], they were selected in order to obtain a sample as homogeneous as possible.

The sample was paired in age with an average of 5.23 years (Mean/5.23-SD/1.99) but not in sex, obtaining 21 children per group. We selected for each group: 5 children of 3 years old, 4 children of 4 years, 4 children of 5 years, 2 children of 6 years, 3 children of 7 years, 2 children of 8 years, 1 children of 10 years old. In the Table 1 the demographic data of the sample are presented. Taking into account that the questionnaire is addressed to parents, we consider another demographic data of interest wish is the degree of schooling of the parents.

The exclusion criteria were addressed to the parents taking into account that they were the ones who contributed the information (parents with developmental or psychiatric disorders, attention deficit, hyperactivity, autistic spectrum disorder). Questionnaires with 20% of the questions without responding or those who did not agree to participate in the study.

With regard to children, the 2- year age group was excluded (due to not having a definite diagnosis of Autism) and children who were receiving some psychostimulant medication, anticonvulsants, or antihistamines, considering that this are medications that can affect the normal architecture of sleep [25]. For the statistical analysis, a database was made using the statistic software 8. The values of p were considered significant below 0.05 and the differences between independent groups were calculated by applying a U Mann Whitney Test.

In Table 2 we show the method of evaluation of the questionnaire, with the items that each sub-scale evaluates, which in turn are in correspondence with sleep disturbances [23]. Sleep behavior is classified on a 3-point scale, 3-usually (5 to 7 times per week) 2-sometimes (2 to 4 times per week) and 1 for rarely (0 to 1 times per week). The punctuation of the items was reversed (1, 2, 3, 11, 26) so that the highest score corresponds to the most disturbed sleep.

Ethical Considerations

All the procedures followed the rules of the Declaration of Helsinki of 2013 for human research, and the study was approved by the scientific and ethics committee (CIREN 63/2015) from the International Center for Neurological Restoration (CIREN). [<https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>]

3. Results

The questionnaires of the autistic children presented the highest values of the total scale with an average of 48.00 while the control group presented an average of 36.47 ($p = 0.00$) (Graph 1)

Significant differences were also found for all the sub-scales of the questionnaire with $p = 0.00$. Only sub-scale 7 did not show statistically significant differences between groups ($p = 0.61$). This sub-scale evaluates sleep-related respiratory disorders, although it is a pathology that usually occurs in relation to the comorbidities that autistic children suffer (obesity) which in this study is not presented. (Table 3)

On the other hand the subscale that evaluates Parasomnias was very affected. This is a sleep disorder that is not the most reported in the literature but is also linked to childhood autism and in all these cases there were significant results ($p = 0.00$) compared to the sleep of healthy controls. We did not find significant differences between the ages of the group of Autistic children and the control group, both with an average of 5.23 (SD/1.99)

Regarding sex, we observed the typical prevalence of male sex described in the literature in the group of autistic children (76%)

Regarding the level of education of parents in both groups, the highest% prevailed in the upper level (67% control group and 62% Autistic group)

Table 1. Socio-demographic characteristics of the sample.

	N	Age Years u(SD)	Sex		Schooling of parents		
			F	M	Low	Medium	Higher
Autistic group	21	5.23 (1.99)	5(23%)	16(76%)	2(9%)	6 (29%)	13 (62%)
Control	21	5.23 (1.99)	12(57%)	9(42%)	0	7 (33%)	14 (67%)

Table 2. Evaluation of the sleep habits survey in children (CSHQ).

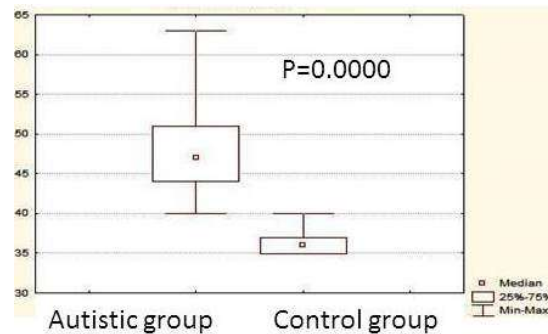
Sub-scales	Items
1 Bedtime resistance	1,3,4,5,6,8
2 Sleep onset	2
3 Sleep duration	9,10,11
4 Anxiety prior to sleep	5,7,8,21
5 Awakenings at night	16,24,25
6 Parasomnias	12,13,14,15,17,22,23
7 Respiratory sleep disorders	18,19,20
8 Daytime drowsiness	26,27,28,29,30,31,32,33

Owens JA, Spirito A, McGuinn M. *The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children.* *Sleep.* 2000; 23:1043-51.

Table 3. Differences between groups for the full scale and sub scales.

	Group 1	Group 2	P-value
Total scale	671.0000	232.0000	0.000000
Sub-scale 1	610.5000	292.5000	0.000063
Sub-scale 2	546.0000	357.0000	0.017444
Sub-scale 3	556.5000	346.5000	0.008258
Sub-scale 4	581.0000	322.0000	0.001123
Sub-scale 5	639.0000	264.0000	0.000002
Sub-scale 6	639.0000	264.0000	0.000002
Sub-scale 7	471.5000	431.5000	0.614884
Sub-scale 8	585.0000	318.0000	0.000784

Comparison between cases of Autistic group (Group 1) and control group (Group 2). (Mean)



Graph 1. Differences between groups for the full scale.

Comparison between cases of Autistic group (Group 1) and control group (Group 2). (Mean / Standard deviation)

4. Discussion

The differences between independent groups showed that sleep disturbances are highly prevalent in the group of children with primary Autism in relation to the control group, which is in congruence with literature. Sleep problems in autisms individuals are related to complex interactions between biological, genetic, psychological, and environmental factors [18].

The autistic group significant differences for all sub scales evaluated by the questionnaire applied. This translates into alterations in sleep onset, sleep duration, anxiety prior to sleep, awakenings at night, Parasomnias with a high level of daytime sleepiness, which has a very negative effect on the daily performance, learning and quality of life of these children and their families.

In these children, clinical characteristics and psychiatric comorbidities, such as pathological anxiety and depression, predispose to sleep problems. Indeed, somatic and cognitive hyper arousal states resulting from rumination and negative thoughts prevent sleep onset [24, 25].

Other causes that predispose sleep problems in children's autism are inadequate sleep hygiene. Conversely, patients with this diagnosis displaying hypersensitivity to tastes or textures may feel more anxious at bedtime, for instance when they brush their teeth, resulting in difficulties to fall asleep [26]. Even, diseases such as epilepsy that may coexist with autism, the medication used (antidepressants, psychostimulants) [27], those related to symptoms associated with autism (Ex. hyperactivity, obsessions, anxiety, stereotypies) that affect sleep and favor the presence of other disorders such as night terrors and sleepwalking [28, 29].

Autistic individuals have difficulties with breaking routines, autism children used to fall asleep in their parents' arms and this is a risk to be unable to fall back to sleep alone after a spontaneous awakening. Similarly, even slight changes in bedtime routine will lead the sleep onset later [30, 31].

Circadian rhythm disturbances in autism children is relate to a socialization deficit. Indeed, the entrainment and the synchronization of the circadian clock depend on zeitgebers such as the social interaction and natural light–dark cycle [32].

In other report (Leu et al. 2011), regarded overnight levels of urinary excretion in this patients appear to be correlated with slow wave sleep and inversely correlated with NREM sleep stage 2 and daytime sleepiness [33].

Regarding clock gene anomalies, studies report mutations in the NLGN/NRXN/SHANK3 (neuroligin/neurexin/synaptic scaffolding protein 3) complex in autistic individuals resulting in sleep-wake disturbances [34].

Recent reports related to the high incidence of insomnia in these patients postulate that the theory of cognitive arousal (thinking and worrying while trying to fall asleep) prevents the initiation of the sleep process. One study showed greater activation of the sympathetic nervous system in patients with insomnia compared to good sleepers [35 - 37].

Thus, we can conclude that there is a high prevalence of sleep problems in the group of children with primary autism compared to the control group. With the exception of sleep-related breathing disorders (sub-scale 7) in the others sub-scales we found significant affectations in the group of children with autism. These evaluate the most common sleep disorders according to the International Sleep Disorders Academy. These disturbances are closely related to complex interactions between biological, genetic, psychological, and environmental factors are implicated in autism spectrum disorder individuals' sleep problems. This is in congruence with what is reported in the updated literature.

The sleep evaluation from a subjective prospect is an alternative to PSG. Questionnaires for parents and caregivers can be used in these patients, through a structured survey. In this, different parameters on quality and behavior during sleep are evaluated. In future studies we propose to complete this evaluation with some objective sleep studies that allows us to investigate in greater depth the sleep disturbances in infantile autism and make new comparisons with patients with sleep disorders and other comorbidities (Ex: epilepsy).

Limitation of the study: We consider that we need to increase our sample in order to relate the sleep disturbances in the specific scales to severity of Autism and socioeconomic status. We neither make any kind of intervention to improve sleep behavior in these children.

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