

## Research Article

# Sleep Characteristics in Patients with Autism Spectrum Disorders

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## Abstract

Autism Spectrum Disorder (ASD) is a heterogeneous, behaviorally defined neurodevelopmental disorder. Patients with ASD might also have co-morbid disorders such as intellectual impairment, epilepsy, and anxiety.

Findings from questionnaire studies have revealed the existence of several sleep problems in pediatric patients with ASD. However, few studies have analyzed the relationship between these disturbances and Polysomnographic (PSG) findings.

On the other hand, about a third of people with autism also suffer from epilepsy. For this reason, long-duration electroencephalograms including an adequate amount of slow wave sleep should be carried out in order to detect epileptiform activity.

The aim of this work is to describe the sleep characteristics and to detect EEG abnormalities in ASD patients using polysomnographic recordings.

**Methods:** Polysomnographic recordings were carried out in 12 autistic children for two consecutive nights and compared to those of the age and sex-matched controls. Sleep efficiency as well as percentages of each sleep phase were obtained from the two groups of participating children. Distribution of SWS and REM sleep throughout the night was also obtained and compared between both groups. Simultaneously, EEG characteristics were analyzed and compared.

**Results:** ASD children presented low sleep efficiency, fragmented sleep and reduction in both SWS and REM sleep. Epileptiform brain activity was observed in 50% of ASD children.

**Conclusion:** ASD patients presented quantitative and qualitative sleep disturbances as well as EEG abnormalities.

## INTRODUCTION

Autism Spectrum Disorder (ASD) is a heterogeneous, behaviorally defined, neurodevelopmental disorder that occurs in 1 of 150 children [1]. Individuals with autism have deficits in social interaction and verbal and nonverbal communication, as well as in restricted or stereotyped patterns of behavior [2]. These patients might also have co-morbid disorders such as intellectual impairment, epilepsy, and anxiety. Epilepsy is associated with pathology of multiple brain regions, among which the cerebral cortex, amygdale, cerebellum, and hippocampal formation are included. These brain regions have also been implicated in autism [1]. Postmortem and magnetic resonance imaging studies have highlighted the frontal lobes, amygdale, and cerebellum as pathological regions in autism. Despite these findings, no unambiguous and consistent pathology has emerged for this neurodevelopmental disorder. Additionally, recent studies emphasize that disturbances in the time course of brain development are fundamental in ASD [3]. It has been suggested

that the heterogeneity of both the core and co-morbid features is related to the heterogeneous pattern of the neuropathology observed in ASD patients.

In this context, defined phenotypes in larger samples of children and well-characterized brain damage are indispensable to elucidate the neuroanatomy of ASD.

The neurological and social deficits observed in autistic patients contribute to varying levels of impairment. Recent advancements in autism research have improved the understanding of the disorder; however, numerous questions about the pathophysiology of ASD remain without precise answers.

The expression of ASD is extremely heterogeneous due to the complex interactions between genes, the central nervous system, and the behavior throughout development. Therefore, some researchers refer to 'the autisms' or ASD rather than a single autism phenotype [4].

Within ASD patients, variability in the social domain ranges from a near absence of interest in interacting with other individuals to slight difficulties managing complex social interactions, where an understanding of other people's goals and intentions and other cues of social context are implicated. Likewise, repetitive behaviors vary from simple motor stereotypies to much more sophisticated rituals, accompanied by emotional disruption when these abnormal behaviors are interrupted. Some patients with ASD lack basic speech abilities, while others have language deficits that are only limited to pragmatic communication. While the majority of individuals with ASD exhibit some level of intellectual impairment, intelligence quotients vary from severely impaired to above average.

On the other hand, sleep disturbances have commonly been described in children with mental handicap [5-7]. Numerous studies have evidenced that sleep problems in autistic mentally retarded children are frequently related to the specific type of syndrome or to its etiological characteristics [8].

In pediatric patients with ASD, findings from questionnaire studies have revealed the existence of several sleep problems with respect to other groups of pediatric patients who have intellectual disabilities [9,10]. Parents of ASD children report a high prevalence of sleep problems, such as difficulty falling asleep, fragmented sleep by frequent awakenings, and reduced total nocturnal sleep time [11]. These sleep disturbances have been hypothesized to have a predictive role in the presence of autistic behavior during the day [12].

While parental sleep concerns have been well documented in children with ASD by means of sleep questionnaires, few studies have related these concerns to Polysomnographic (PSG) findings. Description of PSG abnormalities provides objective evidence of sleep disturbances in these patients.

Although sleep disturbances are not part of the diagnostic criteria for ASD, these disturbances are commonly present in autistic children [12-15]. Additional research is needed to clarify the amount and quality of the sleep problems experienced by these patients compared to those of healthy children [16].

A variety of daytime behaviors related to sleep disturbances for autistic patients has been described. Some authors have suggested that the intensity of developmental disturbances [17] and general ASD symptoms [18] increase in direct proportion to sleeping problems. Studies pointing out the relationships among some of the key diagnostic factors in ASD (e.g., communication difficulties, social problems, stereotypic behaviors, and difficulties breaking routines) have indicated that intensified symptoms in these areas are related to disturbed sleep [12]. Other general daytime troubles such as over activity, psychopathology, disruptive behavior and neurocognitive dysfunction have been related to sleep problems for people with an ASD [19].

On the other hand, about a third of people with autism also suffer from epilepsy. Therefore, long-duration electroencephalograms including an adequate amount of NREM sleep should be carried out in order to detect epileptic form activity. Tuchman and Rapin [20] showed that the incidence of epilepsy in children with autism ranged from 5% to 40% while Hughes and Melyn [21] reported that the electroencephalograms

of 75% of children with autism exhibited abnormal patterns of electrical activity in the brain and 46% had seizures.

The relationship between epilepsy and ASD is poorly understood. It is not known whether epileptic activity in these patients is a secondary phenomenon or whether, in some situations, it is responsible for some symptoms that occur in people with ASD. This is in part why epileptic syndromes are often associated with cognitive, language, and behavioral dysfunction, all of which are traits of this neurodevelopmental disorder.

## Objective

The aim of this work is to describe the sleep characteristics and to detect EEG abnormalities in ASD patients by means of polysomnographic recordings.

## MATERIALS AND METHODS

We followed the guidelines of the Declaration of Helsinki [22] to obtain parent consent of the children selected for the study. In addition, the research project was approved by the ethical committee of the institution where the study took place.

Children with a clinical history of ASD were recruited from a local autism society. Typically, developing children of comparable sex and ages were invited to participate as control subjects. Autistic patients received a clinical diagnosis of ASD from psychologists or clinicians based on parent interviews, children observation, and direct testing. These clinical diagnoses of ASD were verified using the autism diagnostic observation schedule [23]. All autistic children, ages between 4 and 10 years, were not taking psychotropic medications and did not have a history of epileptic seizures or mental retardation.

### Laboratory sleep study

A Grass Comet Model 25 Acquisition System was used to obtain polysomnographic recordings from the 12 autistic children for two consecutive nights. Such recordings were compared to those of the corresponding age- and sex-matched controls. The first night was considered as habituation night; therefore, the data for comparison were those obtained on the second recording night.

All participants had the opportunity to go to bed at their preferred time thus, sleep latencies were not evaluated. Sleep was recorded and scored using 30-s epochs according to standard methods, including central and occipital EEG (C3-A1, C4-A2, O1-A1 and O2-A2), submental EMG, and periorbital EOG [24]. Oronasal airflow and thoracic and abdominal respiratory effort were also monitored throughout the night.

### Statistical analyses

Statistical comparisons were conducted between groups (children with ASD versus their comparison control group) using student's *t*-test and non-parametric Mann-Whitney *u*-tests with significance criteria set at 0.05 level.

Analysis of Variance (ANOVA) on the data obtained per halves of night was also performed to evaluate the distribution of SWS and REM sleep throughout the night.

## RESULTS

During and immediately after electrode placement, some

children with ASD showed anxiety and hyperactivity. Therefore, it was necessary to wait for them to calm down before the polysomnographic recording.

Control children displayed normal sleep distribution throughout the recording night (Figure 1).

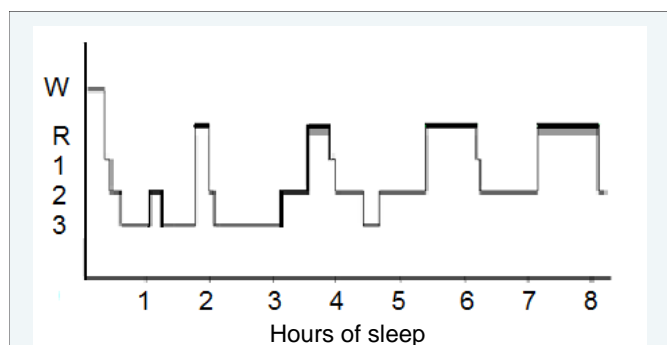
In contrast, atypical characteristics of sleep were displayed by children with ASD. Patients presented fragmented sleep due to frequent interruptions provoked by intermittent awakenings (Figure 2). They also showed more wakefulness after sleep onset, they woke up and fluctuated between wakefulness and sleep stage 1 more frequently than control participants.

Sleep onset and maintenance problems, as well as, early morning awakening resulted in lower sleep efficiency, increased sleep stage 1 and decreased delta sleep (Stage 3 sleep). Total REM sleep time was also reduced. All these variables were significantly different to those in healthy children (Table 1). Some patients with ASD were observed to lie awake for a long time.

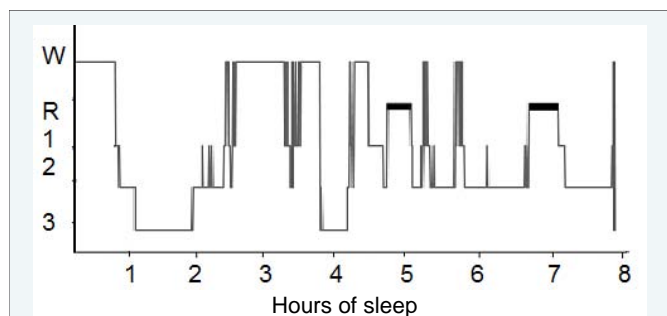
Analyses of sleep stages distribution throughout the night showed that the autistic patients spent significantly more time in sleep stages 1 and 2 during the first half of the night, and less in delta sleep than the control group.

Both, children with ASD and control participants presented more delta sleep in the first half of the night ( $p < 0.05$ ).

The difference in REM sleep distribution was significant



**Figure 1** Hypnogram of a healthy child. Note the normal distribution of sleep. Abbreviations: W: Wakefulness; R: REM sleep; 1, 2 and 3 NREM sleep stages



**Figure 2** Hypnogram of a child with ASD. Disorganization of sleep patterns is observed. Abbreviations: W: Wakefulness; R: REM sleep; 1, 2 and 3 NREM sleep stages

**Table 1:** Means and standard deviations for PSG measures.

Quantitative data of sleep		
	Control (10)	ASD (10)
Total Sleep Time (min)	473.83 (33.26)	369.25 (29.45)*
Stage 1 Sleep (%)	11.19 (0.9)	19.02 (2.8)*
Stage 2 Sleep (%)	48.09 (2.2)	52.82 (4.1)
Stage 3 Sleep (%)	18.94 (1.8)	12.08 (2.1)*
REM Sleep (%)	22.36 (1.71)	16.14 (2.1)*
REM Sleep Duration (min)	18.6 ± 3.4	15.3 ± 5.8
REM Sleep episodes	5.45 (0.93)	3.82 (1.24)*
Sleep Efficiency	90.94%	75.08%*

\* $P < .05$

between the halves of night in patients and in control participants evidenced by an increase in REM sleep in the second half of the night.

The average duration of REM sleep episodes was shorter in patients with ASD (15.3 ± 5.8 min) than in controls (18.6 ± 3.4 min). These patients also showed less REM sleep episodes (Table 1).

On the other hand, although epileptic seizures were absent, 50 % of the studied patients had epileptiform EEG activity during light sleep (Figure 3). The most frequent EEG abnormalities were observed in the central area (C3-A1 and C4-A2 leads) followed by the occipital area (O1-A1, O2-A2 leads).

## DISCUSSION

A considerable amount of polysomnographic studies carried out in children with ASD have focused mainly on abnormalities related to REM sleep [25,26]. Thus, Mahowald and Schenck [27] diagnosed REM sleep behavior disorder without muscle atonia during REM sleep in autistic children who had symptoms of disrupted sleep and nocturnal awakenings [26]. Although we noted a decrease in the amount of REM sleep, we did not observe abnormalities in muscle tone during this sleep phase. The absence of such muscular abnormalities in the autistic children of our study may reflect that they were not under medication. Drugs, usually administered to patients with ASD, such as serotonin reuptake inhibitors may contribute to the lack of muscle atonia, typically present during REM sleep [27].

In agreement with other studies, we observed reduced sleep time, sleep fragmentation provoked by intermittent awakenings, and reduced sleep efficiency. However, our study evidenced an absence of other sleep disorders, such as sleep apnea and parasomnias described by different authors.

Disrupted sleep continuity has been reported, with total sleep time correlating negatively with social and communication abilities [28]. Thus, it is probable that implementation of techniques for sleep continuity may improve these abilities.

On the other hand, it has been hypothesized that both epilepsy and autism [29,30] may result from severe alterations in cortical-subcortical systems connectivity. Alterations in neocortical minicolumns observed in autism support the idea of cerebral under-connectivity [31]. According to Tuchman





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