CHANGES OF SLEEP PATTERNS IN CHILDREN WITH AUTISM SPECTRUM DISORDER – COMPARATIVE STUDY WITH A GENERAL PAEDIATRIC POPULATION

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ABSTRACT

We conducted a descriptive study on a group of 90 subjects divided in two groups: Patients (children diagnosed according to DSM IV TR criteria with Infantile Autism or Atypical Autism) and Control group (children with typical age development selected from Bucharest Sector 4 kindergartens) in order to try to identify different sleep patterns in children with Autism Spectrum Disorder compared with typically developed pediatric population. For ASD assessment we used the ADOS test while the Albany sleep scale was used for checking various sleep disorders. Statistical analysis was performed using SPSS Statistics version 20. The most common changes of sleep patterns in children with Autism Spectrum Disorders are caused by poor sleep hygiene and dysfunction of circadian rhythm (p = 0.01), sleep related movement disorders (p = 0.006) and sleep related breathing disorders (p = 0.002), bruxism (p = 0.004) and nocturnal enuresis. The new element brought by this study is the analysis of correlation between the frequencies of different sleep disorders found in children with Autism Spectrum Disorders. Thus it appears that poor Sleep hygiene/routines are most often affected in these subjects by increased frequencies of Sleep Related Movement Disorders (p = 0.01). The frequency of Night Awakenings in patients with Atypical Autism was linked to Sleep Related Breathing Disorders (p = 0.013), Sleep Related Movement Disorders (p = 0.011) and Sleep Anxiety (p = 0.009). Sleep disorders are frequent comorbidities among children with ASD compared to typically developing children and although there is no real difference to their distribution between subjects with Infantile Autism and Atypical Autism we may outline a profile of sleep patterns in these subjects.

Keywords: Autism spectrum disorder, Autism, sleep disorders.

INTRODUCTION

Autism spectrum disorders (ASD) are a group of psychiatric disorders with similar symptoms, but which varies in severity, from mild to severe forms, and so they represent a continuum rather than different diseases [1]. ASD according to the DSM V is defined by qualitative impairments in communication and social interactions, restricted interests and activities, and stereotypical behaviors [2].

ICD-10 uses the name of Pervasive Developmental Disorders to define a group of psychiatric disorders characterized by impairments in both social and emotional interaction, communication impairments and a difficult flexibility in thinking and behavior that leads to restricted, repetitive, and stereotyped patterns of behavior, interests, and activities [3].

Children with ASD present frequent psychiatric and medical comorbidities. Studies show that up to 41% of children with ASD have psychiatric comorbidities, of which the most common are intellectual disabilities, ADHD, Anxiety and Mood disorders, as well as oppositional defiant disorders [4, 5]. Among medical comorbidities a high prevalence is observed in sleep disorders, epilepsy and gastrointestinal problems [6].
Sleep disorder is an "umbrella" term covering a variety of phenotypes (manifestations) in sleep disorders. According to ICSD-2 (International Classification of Sleep Disorders-Second Edition: Diagnostic and Coding Manual) we consider that there is a sleep disorder when the inability to sleep leads to inadequate functioning during the day or to a state of excessive daytime sleepiness [7].

Sleep disorders are a real and important problem for children with autism spectrum disorders that should be assessed through routine clinical checkup because of the high prevalence and negative impact on the quality of life in these children and their families. Sleep disorders affect approximately 20 to 30 % of the general pediatric population. In the ASD population the prevalence is much higher and is estimated at between 44 and 86 % [8; 9; 10].

The most commonly reported problems in these children are insomnia (40-80%), which can include inability to initiate sleep and difficulty maintaining sleep, circadian rhythm disorder (4-35%) and bruxism [10]. The most common symptoms of sleep disorders in children with ASD are irritability, hyperactivity, cognitive dysfunctions (memory, attention, concentration), excessive daytime sleepiness, stereotypes exacerbating or executive functions deficits [11] and these symptoms are secondary to delayed sleep onset and the decrease in total sleep time/24 hours, frequent night awakenings [12, 13], dysfunctions in sleep-wake rhythm through the presence of "bad" sleep routines [14]. Sleep disorders in children with ASD are frequently associated with exacerbation of autistic symptoms, but there is yet no evidence that argues for a direct causal relationship between the two of them [15; 16].

The etiology of sleep problems in children with ASD is likely multifactorial, including genetic, biological and environmental factors as well as medical and behavioral conditions. Among the main factors contributing to the occurrence of these disorders there are disruptions in the sleep-wake cycle, melatonin production dysfunction (elevated melatonin levels during the day and decreased levels of melatonin at night) [10, 20-22] and genetic - mutations in genes that control the production of Acetylserotonin O-methyltransferase (ASMT – last enzyme involved in melatonin synthesis) [23].

Sleep patterns in the ASD can be investigated using questionnaires (Children's Sleep Habits Questionnaire – CSHQ / ALBANY scale / BEARS Sleep Problems Scale) or through objective clinical assessment that includes the actigraph and clinical polysomnography [10].

Children with ASD are the "main group of beneficiaries" for the pharmacological sleep therapy according to the American Academy of Pediatrics [24, 10], although they do recommend that the first-line in treating Sleep Disorders in children with ASD should be behavioral therapy and only in the absence of any favorable results, doctors should think of pharmacological treatment aids [25].

**OBJECTIVE**

This study aims to identify abnormal patterns of sleep in children with Autism Spectrum Disorders compared to typically developed pediatric population, but also comparing Infantile Autism (IA) and Atypical Autism (AA) sleep patterns (differences and similarities) which will allow us to outline a sleep profile in these subjects. The study checks also for correlations between the frequencies of various sleep disorders in the autism spectrum disorders children population.

The working hypothesis was that sleep disorders are more likely to occur among children with ASD compared to children with typical development in stage ages, which is consistent with literature data from other studies [8-10]. The second working hypothesis was that within ASD there's a different rapport of sleep...
disorder between subjects with Atypical Autism and those with Infantile Autism, but also that the frequencies of some of these sleep disorders can correlate either with each other or with individual characteristics, which helped shape a sleep profile in these subjects.

**METHOD**

**Participants**

90 subjects evaluated between 4.01.2013-20.06.2013. From the start the sample was divided into two study groups (Group I - Patients, Group II - Control/Witnesses). Study group I - 50 subjects, male and female, aged between 2 and 14 years; subjects in this group are patients in the Child and Adolescent Psychiatry Department from "Prof. Dr. Alexander Obregia" Psychiatry Hospital diagnosed with Infantile Autism or Atypical Autism according to DSM IV TR criteria; the diagnosis was instrumented using ADOS test. Study group II - 40 subjects, male and female, between the ages of 2 and 12 years old; subjects in this group belong to the pediatric population with typical development in age stages and were evaluated in Bucharest Sector 4 kindergartens. Data was collected at the presentation time at the hospital/kindergarten.

**Assessments instruments**

**ADOS assessment**

ADOS (Autism Diagnostic Observation Schedule) is a standardized protocol used for the assessment of individuals who have been referred for further testing secondary to the suspicion of possible autism or an autistic spectrum disorder. The test can be applied to children over the age of two and has been applied to Study Group I by an examiner (psychologist/physician) with special training in administrating the test. ADOS consists of 4 modules, each with an average duration of 30 minutes, and each module is addressed to different individuals, depending on their expressive language level and chronological age. The test consists of four investigated areas, depending on the studied behavior: Communication, Social interaction, Stereotyped Behaviors and Game; for each task the examiner gives a score between 0 (absence of abnormal behavior) and 3 (maximum severity in behavioral abnormalities); the results are summed up and conclude to a score for each of the four areas investigated. In addition, the scores for communication and social interaction are summed up resulting a Total ADOS score with which, based also on clinical context, the subject is included in two categories: Infantile Autism and Atypical Autism.

**Sleep disorders assessment**

Albany scale is a questionnaire that assesses the presence of sleep disorders and their various types in children. The questionnaire consists of 46 questions and is addressed to parents; it can be applied by both medical staff/psychologists or parents. The questionnaire includes questions with pre-formulated answers, but also open questions for which the respondent must complete the answer depending on the situation. Answers are grouped into categories: Sleep hygiene and schedule, Medications, Daytime sleepiness, Sleepwalking, Nightmares, Night terrors, Hypersomnia and Narcolepsy, Sleep related Breathing Disorders and Movement Disorders, Nocturnal enuresis, Bruxism, Sleep anxiety.

For questions with pre-formulated answers we calculate a score between 0-4, depending on the frequency of the behavior/activity surveyed. For Yes/No/Don't know questions the responses are coded with 0 or 1 scores, depending on the question relevance. To facilitate statistical analysis questions are grouped into areas, and each area is given a score obtained from the sum of the most representative questions that investigate that area. Thus we have the following groups/domains (G1)- Sleep hygiene and routines; (G2)-Night awakenings; (G3) - Hypersomnia/Narcolepsy; (G4) - Sleep Related Breathing Disorders; (G5) - Sleep Related Movement Disorders; (G6) - Sleep Anxiety; (G7)- Bruxism; (G8) – Nocturnal Enurezis.

**Statistical analysis**

In order to create the database and perform statistical analysis of data a SPSS Statistics 20.0 program has been used. Descriptive statistics and graphics were used in characterizing the batches. For sleep disorder comparisons between the two groups, but also within Group I we have applied the Mann -
Whitney U statistical test and Kruskall - Wallis test for non-gaussian distributions. The relationship between variables is verified using Spearman Correlation Coefficient (non-parametric equivalent of the Pearson Correlation Coefficient, used in comparing two quantitative variables with non-gaussian distribution).

RESULTS

Descriptive statistics
The two groups examined do not differ very much in age as it is pointed out by the comparative descriptive statistics (Table II). Within Group I we notice the absence of any significant statistical differences between age means in subjects with Infantile Autism - IA and Atypical Autism- AA (Table III). Sex ratio (Male/Female) in Group I is 4/1, and in Group II is 1/1 (Table I). As a result of applying ADOS in Group I-Patients (n = 50) we have observed a higher percentage of subjects with Atypical Autism -76% compared to those with Infantile Autism -24% (Figure 1). Obtaining the score 7 in ADOS test was considered suggestive for framing the subjects in the Autism Spectrum Disorders group.

Table I. Gender distribution depending on study Groups - absolute values

<table>
<thead>
<tr>
<th>Group * Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I – ASD  N=50</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Group II – Control N=40</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

Table II. Descriptive statistics - age comparison between the groups

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>Mean</td>
<td>4.82</td>
<td>4.83</td>
</tr>
<tr>
<td>Median</td>
<td>4.00</td>
<td>4.50</td>
</tr>
<tr>
<td>Module</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Minimum</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Maximum</td>
<td>14</td>
<td>12</td>
</tr>
</tbody>
</table>

Table III. Descriptive statistics of age in Group I, depending on diagnosis

<table>
<thead>
<tr>
<th>Age *Diagnosis</th>
<th>N</th>
<th>Mean</th>
<th>Module</th>
<th>Med.</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile Autism</td>
<td>12</td>
<td>5.17</td>
<td>3</td>
<td>4.50</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Atypical Autism</td>
<td>38</td>
<td>4.71</td>
<td>4</td>
<td>4.00</td>
<td>2</td>
<td>14</td>
</tr>
</tbody>
</table>

Figure 1. Group I distribution according to ADOS classification.

Albany scale results and comparative study of sleep disorders between the two groups

G1: Sleep hygiene and routines

After applying the Mann-Whitney U test (U=210.000; p=0.68) we can preserve the null hypothesis according to which there is no significant statistical difference in the frequency of sleep routines and sleep hygiene among individuals with Infantile Autism and Atypical Autism.

Table IV. Kruskall-Wallis test for score comparison G1: Sleep hygiene and routines among the three groups (IA/AA/Control)

<table>
<thead>
<tr>
<th></th>
<th>H_{kw}</th>
<th>Df</th>
<th>Asymp. Sig. (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1: Sleep hygiene and routines</td>
<td>13.278</td>
<td>2</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Sleep disorders caused by poor sleep routines and hygiene are more common among individuals with ASD (p = 0.001) and are
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 caused by a higher frequency of sleep-resistance (≈ 20%, n = 50, 9/50) compared to the control group (2.5%, n = 40, 1/40) (Figure 3).

Among subjects with Infantile Autism they seem to be related to an inexistent regular sleep schedule (30% vs. 62%) compared to the control group.

For a better view of the differences between the three groups we used a box-plot diagram (Figure 4), where the high variation of Night Awakenings among subjects with ASD is observed.

In terms of Hypersomnia/Narcolepsy, but also Sleep Related Respiratory Disorders we did not identify differences in frequency distribution among the subjects from Group I (Table VI).

These sleep disorders are much more common in individuals with ASD than general pediatric population as the Kruskall-Wallis test shows (H_{kw} = 12,174; p = 0.002 for G3 scores and H_{kw} = 12,288; p = 0.002 for G4 scores); furthermore after applying the Mann-Whitney test with adjustment of p (Bonferroni p = 0.025) we have identified a significant statistical difference in both paired groups (Table VII) for Hypersomnia/Narcolepsies and significant difference between the Infantile Autism group and the control group for Sleep Related Respiratory Disorders (Figures 5 and 6).

Figure 2. G1 score (Sleep hygiene and routines) distribution depending on the Study Group

Table V. Mann-Whitney U Test comparing G2 scores: Night Awakenings, depending on pair-groups (IA/AA/Control)

<table>
<thead>
<tr>
<th>Group 1 – Group 2</th>
<th>Mann – Whitney U</th>
<th>Asym. Sig (p)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control – AA</td>
<td>450.000</td>
<td>0.001</td>
</tr>
<tr>
<td>Control – IA</td>
<td>154.500</td>
<td>0.050</td>
</tr>
</tbody>
</table>

* adjusted P = 0.025. Statistically significant at a p value < 0.025.
However it appears that approximately 21% (n = 38, 8/38) of subjects with Atypical Autism presents falling asleep anxiety for at least 3-6 times/night compared to the control group (10%, n = 40, 4/40) and subjects with Infantile Autism (≈ 8%, n = 12, 1/12) (Figure 8).

G7 = Bruxism; G8 = Nocturnal Enuresis
Bruxism (Figure 9) has the highest frequency among subjects with Atypical Autism (≈ 20%, n = 38, 8/38) and Infantile Autism (16%, n = 12, 2/12) compared to the control group (5%, n = 40, 2/40), as shown by the Kruskall-Wallis test ($H_{KW} = 10.591; p=0.004$). In the case of Nocturnal Enuresis ($H_{KW} = 15.823; p=0.0003$) it is noted that the highest frequency is observed among subjects with Atypical Autism (35%, n = 38, 12/12) compared to the control group (5 per cent, n = 40, 2/40) (Figure 10).

G5: Sleep Related Movement Disorders;
G6: Sleep Anxiety
Sleep Related Movement Disorders have a higher frequency among subjects with Autism Spectrum Disorders compared to the control group (Figure 7) as it results from the Kruskall-Wallis test ($H_{KW} = 10.247; p=0.006$). In terms of Sleep Anxiety we have not found statistically significant differences ($H_{KW} = 1.499; p=0.473$) between G6 scores depending on groups.
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**Figure 7.** G5 scores: Sleep Related Movement Disorders scores distribution depending on groups

**Figure 8.** Sleep Anxiety frequency depending on group

**Figure 9.** Compared bruxism frequencies between the three groups.

**Figure 10.** Compared Nocturnal Enuresis frequencies between the groups of subjects

Correlation between frequencies of different types of sleep disorders

Table VIII. Correlations between frequencies of different types of sleep disorders depending on the groups.

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Variables</th>
<th>Results of Spearman Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>G1, G5</td>
<td>$r_s = 0.612, p = 0.002$</td>
</tr>
<tr>
<td></td>
<td>G1, G6</td>
<td>$r_s = 0.602, p = 0.0003$</td>
</tr>
<tr>
<td></td>
<td>G2, G5</td>
<td>$r_s = 0.449, p = 0.004$</td>
</tr>
<tr>
<td></td>
<td>G6</td>
<td>$r_s = 0.557, p = 0.0001$</td>
</tr>
<tr>
<td></td>
<td>G3–G4</td>
<td>$r_s = 0.529, p = 0.0004$</td>
</tr>
<tr>
<td></td>
<td>G5–G6</td>
<td>$r_s = 0.553, p = 0.0002$</td>
</tr>
<tr>
<td>Atypical Autism (AA)</td>
<td>G1–G5</td>
<td>$r_s = 0.417, p = 0.009$</td>
</tr>
<tr>
<td></td>
<td>G2, G4</td>
<td>$r_s = 0.398, p = 0.013$</td>
</tr>
<tr>
<td></td>
<td>G5</td>
<td>$r_s = 0.408, p = 0.011$</td>
</tr>
<tr>
<td></td>
<td>G6</td>
<td>$r_s = 0.416, p = 0.009$</td>
</tr>
<tr>
<td></td>
<td>G4, G5</td>
<td>$r_s = 0.499, p = 0.004$</td>
</tr>
<tr>
<td></td>
<td>G6</td>
<td>$r_s = 0.437, p = 0.006$</td>
</tr>
<tr>
<td>Infantile Autism (IA)</td>
<td>G1–G5</td>
<td>$r_s = 0.538, p = 0.003$</td>
</tr>
<tr>
<td></td>
<td>G5–G6</td>
<td>$r_s = -0.700, p = 0.011$</td>
</tr>
</tbody>
</table>

G1: Sleep hygiene and routines, G2 = Night Awakenings, G3 = Hypersomnia/Narcolepsy, G4 = Sleep Related Breathing Disorders, G5 = Sleep Related Movement Disorders, G6 = Sleep Anxiety.

**DISCUSSIONS**

Although there is no real significant statistical difference of various sleep disorders distribution between subjects with Infantile Autism and Atypical Autism, we can outline a sleep profile in these subjects. This is observed
in sleep routines in participants with AA, among whom there is a higher percentage of subjects with a regular sleep schedule and good sleep hygiene, compared to those with Infantile Autism. Also, in the case of subjects with Atypical Autism there is a higher percentage in frequency of Night Awakenings (≈ 28%, n = 38, 11/38) compared to subjects with Infantile Autism (≈ 8%, n = 12, 1/12). However, statistical tests do not find a significant statistical difference in sleep disorders (p = 0.082) between these two categories of children with ASD. In the case of Hypersomnia/Narcolepsies it is noted that there is a significant statistical difference (p = 0.002) between the control group and Group I, with a clear predominance of these types of sleep disorders among subjects with Autism Spectrum Disorders. The same results is obtained for Sleep Related Breathing Disorders (p = 0.002) with a higher level of occurrence of these types of sleep disorders among subjects with Autism Spectrum Disorders. In terms of Sleep Anxiety we have not found statistically significant differences (p = 0.473) between the G6 scores depending on batches. However it appears that approximately 18% (n = 50, 9/50) of the subjects with ASD exhibit falling asleep anxiety for at least 3-6 times/night compared to the control group (10%, n = 40, 4/40). Bruxism and Nocturnal Enuresis are much more common among subjects with ASD (n = 50; 20%, 10/50 for Bruxism and 36%, 18/50 for Enuresis) compared to the control group (5%, n = 40, 2/40 for both disorders), as it is shown also by the Kruskall-Wallis test (p = 0.004).

The most common changes of sleep patterns in children with Autism Spectrum Disorders are caused by poor sleep hygiene and dysfunction of circadian rhythm, sleep related movement disorders and sleep related breathing disorders, bruxism and nocturnal enuresis. These data is consistent with other literature data [8- 10, 12, 14]. The new element brought by this study is the analysis of correlation between the frequencies of different sleep disorders found in children with Autism Spectrum Disorders. Thus it appears that poor Sleep hygiene/routines are most often affected in these subjects by increased frequencies of Sleep Related Movement Disorders. The frequency of Night Awakenings in patients with Atypical Autism was linked to Sleep Related Breathing Disorders, Sleep Related Movement Disorders and Sleep Anxiety.

An unexpected result in the Group of subjects with Atypical Autism is that of linking Sleep Related Breathing Disorders with Sleep Anxiety and Sleep Related Movement Disorders. In other words the falling-asleep Anxiety and Sleep Related Movement Disorders are more frequent as the incidence of Sleep Related Breathing Disorders in children with Atypical Autism increases.

In the control group we observed that the disruption of routine sleep is directly related to the frequency of Sleep Related Movement Disorders, but also with Sleep Anxiety. Night awakenings in this batch are caused by the same sleep disorders affecting the sleep hygiene/routines, but in addition obtaining a positive correlation between Hypersomnia/Narcolepsy and Sleep Related Movement Disorders draws attention to a possible poor diagnosis /lack of additional investigation of respiratory problems which can cause sleep disorder in general pediatric population.

**Limitations**

Interpretation of this study results should be done taking into account the methodological limitations caused by the small number of subjects who participated in the study, the lack of objective laboratory investigation and the subjective approach of clinical symptoms that are reported by parents.

**CONCLUSIONS**

The most common changes of sleep patterns in children with Autism Spectrum Disorders are caused by poor sleep hygiene and dysfunction of circadian rhythm, sleep related movement disorders and sleep related breathing disorders, bruxism and nocturnal enuresis. These data is consistent with other literature data [8- 10, 12, 14]. The new element brought by this study is the analysis of correlation between the frequencies of different sleep disorders found in children with Autism Spectrum Disorders. Thus it appears that poor Sleep hygiene/routines are most often affected in these subjects by increased frequencies of Sleep Related Movement Disorders. The frequency of Night Awakenings in patients with Atypical Autism was linked to Sleep Related Breathing Disorders, Sleep Related Movement Disorders and Sleep Anxiety.

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**CONCLUSIONS**

The most common changes of sleep patterns in children with Autism Spectrum Disorders are caused by poor sleep hygiene and dysfunction of circadian rhythm, sleep related movement disorders and sleep related breathing disorders, bruxism and nocturnal enuresis.

There is no real difference in sleep disorders distribution between subjects with Autism Infantile and Atypical Autism; however we can outline a particular sleep profile in these subjects.
The sleep profile of children with Infantile Autism assumes the existence of the lowest frequency in sleep schedule compared to subjects with Atypical Autism or pediatric population with typical development.

The quality of the sleep in children with Atypical Autism is affected by the high frequency of night awakenings, which in turn is directly linked to an increased frequency of Sleep related breathing disorders or Sleep related movement disorders. Sleep anxiety disorders, but also Sleep related movement disorders are much more common among subjects with Atypical Autism that seem to have Sleep related breathing disorders among the comorbidities.

REFERENCES


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