Sleep Disturbances as a Manifestation of Neurodevelopmental Disorders

Abstract:

Sleep disturbances are complex elements of many neurodevelopmental disorders, such as autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD),intellectualanddevelopmentaldisabilities, and insomnia. Sleep disturbances are caused by a variety of factors, resulting in short-term and long-term consequences that can affect self-care, daily functions, and well-being. Sleepdisturbancescan compromise not only he general health of individuals but also on the health of caregivers and support systems. There is a need to understand the interaction between neurodevelopmental disorders and sleep disturbances to toidentify patterns of sleep fragmentations contributed to neurobiological and neurodevelopmental conditions, determine appropriate treatment, improve the quality of life for individuals with neurological comorbidities.

1) Introduction:

Sleep disturbance is a typical area of focus reported by parents to their children's pediatrician. Approximately 25 % of typically developing preschool-aged children suffer sleep conditions due to sleep start delays and nocturnal awakenings [1, 2]. Sleep problems in children with neurodevelopmental disorders (NDD) are significantly more widespread. In NDD, the prevalence of sleep disturbances has been reported to be as high as 86 % [3]. Sleep problems are included in the diagnostic criteria for many NDDs, encompassing several medical and psychiatric conditions .The prevalence of sleep disturbances is higher in growing children, and unlike typically developing persons, sleep abnormalities in children with NDD commonly linger into adolescence and adulthood [4].

The etiology of sleep disruptions in neurodevelopmental disorders (NDD) is characterized by the involvement of many factors. Sleep disturbances can arise from various factors, including medical and neurological disorders such as gastroesophageal reflux and epileptic seizures,

behavioral issues like inadequate sleep hygiene and environmental factors, the use of medications, psychiatric disorders like depression, bipolar disorder, and post-traumatic stress disorder, and specific sleep disorders such as obstructive sleep apnea and restless legs syndrome. Diverse interventions may be necessary to address sleep and behavioral difficulties in children with distinct developmental impairments. Some individuals may require additional melatonin supplementation for the management of insomnia or circadian rhythm abnormalities, whereas others may necessitate interventions targeting obstructive sleep apnea. Sleep disturbances commonly observed in neurodevelopmental disorders (NDD) may be associated with two primary issues: insomnia, which encompasses difficulties with both initiating and maintaining sleep, and hypersomnia [5-9].

1.1. The Complex Relationship Between Sleep and Neurodevelopmental Disorders

Sleep disturbances in individuals with neurodevelopmental disorders are often multifaceted. They can be attributed to various factors, including genetic predispositions, altered circadian rhythms, sensory sensitivities, anxiety, and behavioral difficulties. These factors may interact and compound the sleep issues faced by these individuals[10, 11].

1.1.1. **Autism Spectrum Disorder** :

Children with Autism Spectrum Disorder (ASD) frequently experience sleep disturbances, with problems of difficulty falling asleep, frequent awakenings during the night, and early morning waking. These issues can exacerbate the core symptoms of ASD, such as impaired social interaction, communication difficulties, and repetitive behaviors. Although the exact cause of sleep disturbances in ASD is not fully understood, ASD thought to be related to atypical neural functioning and sensory sensitivities. Sensory overstimulation or hypersensitivity to sensory stimuli can make falling and staying asleep a significant challenge for individuals with ASD[12].

1.1.2. **Attention-DeficitHyperactivity Disorder**:

Sleep disturbances are also common in individuals with Attention-deficit hyperactivity disorder (ADHD). Individuals may struggle with hyperactivity, impulsivity, and inattention during the day, which can lead to bedtime resistance and difficulty falling and staying asleep at night.

Moreover, individuals with ADHD might experience restless leg syndrome, periodic limb movement disorder, and other sleep-related conditions that further disrupt their sleep patterns[13, 14].

1.1.3. **Intellectual Developmental Disabilities**:

Individuals with intellectual developmental disabilities often have a higher prevalence of sleep disturbances. They may experience difficulties with self-soothing, communication, and understanding bedtime routines, making it challenging for caregivers to establish regular sleep patterns. These sleep issues can compound the challenges that individuals with intellectual disabilities already face in their daily lives[15-17].

2. Sleep Disorders In People With Intellectual Developmental Disability

Sleep disturbances are frequently observed among individuals with intellectual developmental disabilities, as evidenced by the prevalence rates of sleep difficulties in children ranging from 24% to 86% [18]. The prevalence of sleep disturbances among persons with intellectual developmental disabilities is reported to range from 8.5% to 34.1%, with a notable 9.2% suffering substantial sleep difficulties. A significant proportion of older adults with an intellectual developmental disability, specifically 72% out of a sample size of 551 individuals in a study, experienced sleep issues [18, 19].

The investigation of mental and physical health conditions and their corresponding therapy in individuals with intellectual developmental disabilities is an area that has received limited attention. Diagnostic and management procedures are frequently derived from research conducted on individuals who do not have intellectual developmental disability. Sleep disturbances in persons with intellectual impairments may have a consistent pattern The limited data available on the etiology and consequences of sleep issues in individuals with intellectual developmental disorders highlightsthe need for further investigation and intervention in this area [20]. Gaining insight into the various sleep issues encountered by persons with intellectual impairments and comprehending the multitude of factors that impact their sleep can contribute to the evaluation and treatment of sleep difficulties in this population [21].

There exist multiple plausible rationales for the heightened prevalence of sleep disturbances among adults with intellectual developmental disabilities. .. A systematic review conducted on sleep disturbances in persons with intellectual impairments revealed significant correlations between sleep patterns and several characteristics such as challenging behavior, the use of psychotropic medication, mental health issues, and respiratory diseases [22].

3. Neurodevelopmental Conditions

Autism spectrum disorder (ASD) frequently co-occurs with intellectual developmental disabilities, presenting as a comorbidity. The prevalence of ASD in persons with moderate to profound intellectual disability can reach up to 39% [23]. Individuals with ASD frequently experience chronic sleep disturbances throughout their lifespan. A comparative analysis of circadian rhythms and sleep patterns in persons diagnosed with ASD and intellectual difficulties was compared to a control group of typically developing adults and identified a correlation [24]. The results of study revealed that adults diagnosed with ASD and intellectual developmental disabilities have an extended period of time before falling asleep, more frequent and longer awakenings during the night, and reduced effectiveness of sleep when compared to adults who do not have a neurodevelopmental disorders. The multifaceted origins of sleep difficulties in individuals with ASD [26], and several factors contribute to biological irregularities in the timing of melatonin release and disruptions in sleep patterns resulting from concurrent medical and mental illnesses [25].

Attention-deficit hyperactivity disorder (ADHD) is a complex condition that affects brain activity and functions. Individuals with intellectual disabilities have a greater incidence of ADHD compared to those without intellectual developmental disabilities, with reported rates reaching as high as 19.6%. Sleep disturbances are a prevalent concern that impacts those diagnosed with ADHD, with documented prevalence rates reaching as high as 50% among this population. Numerous hypotheses exists to elucidate the underlying causes of sleep disturbances in individuals with ADHD. A multifaceted association between sleep and ADHD suggests that disrupted sleep may be an inherent characteristic of ADHD, which is further influenced by the impact of psychostimulant treatment [28]. Despite the established correlation, sleep difficulties

associated with ADHD may be categorized as a challenging condition to understand " among persons who also have co-occurring intellectual developmental disability.

4. Genetic Conditions

In recent times, there has been notable advancement in r comprehending the fundamental genetic components contributing to the onset of intellectual impairments. The distinctive attributes of Down's syndrome encompass hypotonia, obesity, and craniofacial anomalies, all of which heighten the susceptibility to sleep-disordered breathing conditions, such as obstructive sleep apnea (OSA). Individuals diagnosed with cri du chat syndrome exhibit a heightened susceptibility to the development of OSA. Individuals diagnosed with Smith-Magenis syndrome exhibit an elevated susceptibility to circadian sleep-wake disorders, commonly characterized by an inverted sleep-wake cycle that is believed to arise from an abnormality in the melatonin system [26-29].

5. Psychological And Environmental Factors

Sleep disruption frequently serves as a first indicator of declining mental well-being among individuals with mental illness, whereas inadequate sleep is a fundamental manifestation of numerous affective and psychotic disorders. The elevated occurrence of sleep problems among individuals with intellectual impairments can be comprehended within the framework of the heightened frequency of mental illnesses in this population, relative to individuals without intellectual developmental disabilities [30, 31].

The consideration of the environment's influence on the development of sleep disorders is a crucial aspect in determining the underlying causes of sleep issues in individuals with intellectual developmental disabilities. Sleep cycles of individuals in residential homes may be compromised due to nocturnal staff check-ins, which can lead to heightened levels of interactions and lights that disrupt the sleep patterns of residents[35]. Additional environmental factors that should be taken into account for individuals residing in supported living facilities encompass the potential presence of cohabitants experiencing sleep disturbances, which may result in disruptive

nocturnal noises. Furthermore, the limited availability of outdoor activities that facilitate exposure to natural light should be considered. **The Impact of Sleep Disturbances**:

Sleep disturbances can have a profound impact on the daily lives of individuals with neurodevelopmental disorders. The consequences of poor sleep quality are far-reaching and may include[32-34]:

- Cognitive Impairments: Sleep disturbances can exacerbate cognitive impairments in individuals with neurodevelopmental disorders, affecting their learning and overall development.
- Behavioral Problems: Poor sleep can lead to increased irritability and challenging behaviors, which can further disrupt family dynamics.
- Impaired Quality of Life: For both individuals and their families, sleep disturbances can contribute to a decreased quality of life and increased stress.

6. Analysis of Phenotypes for Sleep Disorder

Various sleep assessment approaches should be tailored to suit the individual needs of each child. Parent-reported questionnaires and sleep diaries are commonly utilized subjective tools in the examination of sleep problems..The key benefits associated with these approaches is the non-invasive nature that allows for the collection of data without causing harm or discomfort to the child as well as the cost-effectiveness of journaling sleep activities. The Children's Sleep Habits Questionnaire (CSHQ) is widely recognized as a prominent survey completed by parents whereby the questionnaire is designed to evaluate the sleep patterns of school-aged children through the collection of information provided by parents. Another technique that can be employed is Electroencephalography (EEG)that requires the attachment of two electrodes to a patient's scalp. The device offers a comprehensive record of the brain's EEG patterns throughout both sleep and periods of reduced physical strength. The polysomnogram (PSG) approach is widely recognized as the standard for objectively evaluating sleep, in contrast to a single-channel EEG. The assessment includes physiological indicators of both typical and atypical brain electrical patterns, the structure of sleep, the various stages of sleep, the overall quality of sleep, as well as eye movements and bodily movements exhibited during sleep. Actigraphy is a method that allows for the assessment of limb activity in a non-invasive mannerthat is achieved by

utilizing an accelerometer to detect and distinguish periods of sleep and alertness. The actigraphy technology facilitates the gathering of data over extended periods of time inside unstructured environments. The study investigated the reliability of actigraphy in conjunction with polysomnography (PSG) and found a robust correlation (>0.80) between PSG and actigraphy measurements for sleep latency, duration, and efficiency A citation is needed).Videosomnography, akin to actigraphy, derives its advantages from its ability to provide objective documentation over an extended duration. Though the utilization of videosomnography in the field of child sleep research has various challenges[35-40],it has the capability to document atypical events such as parasomnias that occur during the nighttime[39-44. .

7. **Addressing Sleep Disturbances In Neurodevelopmental Disorders**:

Managing sleep disturbances in individuals with neurodevelopmental disorders can be complex and requires a tailored approach. Some strategies to consider include:

- Behavioral Interventions: Implementing consistent bedtime routines and positive reinforcement for good sleep behavior can be effective.
- Medication: In some cases, medication may be prescribed to manage specific sleep-related issues, such as insomnia or restless leg syndrome.
- Sensory Accommodations: For individuals with sensory sensitivities, creating a sleep environment that minimizes sensory triggers can be helpful.
- Therapies: Behavioral therapy and social stories can be used to help individuals with neurodevelopmental disorders understand and follow sleep routines.
- Collaboration: Working with healthcare professionals, including pediatricians, sleep specialists, and therapists, can provide valuable insights and strategies for managing sleep disturbances.

Early and frequent screenings for sleep impairment and its related conditions are recommended.

7.1. **Non-Pharmacological Management:** The management of sleep problems in children and adolescents diagnosed with Autism Spectrum Disorder (ASD) necessitates a comprehensive approach that addresses both environmental and behavioral factors. Parents should establish consistent sleep habits and provide a conducive bedroom

environment for their children. The implementation of environmental and behavioral interventions can enhance sleep quality, though may posesome challenges in their practical application for some children with difficulty adhering to sleep regimes. The Sleep Committee of the Autism Treatment Network devised a specialized behavioral modification tool known as the sleep tool kit (STK) to address sleeplessness in children and adolescents. The STK framework proposes three strategies: the implementation of visual schedules to promote appropriate evening behaviors, the incorporation of a supplementary relaxation module to decrease levels of arousal, and the gradual fading of nighttime routines to facilitate sleep onset while experiencing fatigue. Various adjunctive interventions including as breathing methods, muscular relaxation exercises, yoga, massage, mindfulness training, and warm baths have been found to be beneficial in assisting patients in managing their levels of arousal and anxiety. Considering the developmental attributes of children with ASD, research indicates that implementing positive routines, employing unmodified and progressive extinction techniques, and utilizing overnight fading strategies are particularly advantageous for children aged 5 and below. For older children and adolescents, cognitive-behavioral therapy (CBT) has been found to yield greater benefits [41-45].

7.2. **Pharmacological Management:** Medical intervention is deemed necessary in cases where children do not exhibit positive responses to behavioral therapy.

7.3. **Role of Melatonin:**Individuals with Autism Spectrum Disorder may experience sleep issues and changes in their circadian rhythm due to a reduced level of sociability [50-52]. Certainly, zeitgebers, which are sometimes referred to as timeivers, play a crucial role in the entrainment and synchronization of the circadian clock. Examples of these zeitgebers are the natural light-dark cycle, music, and social cues. Individuals diagnosed with ASD may experience difficulties in seeing or interpreting social cues, which can potentially hinder the functionality of mechanisms responsible for regulating sleep and wakefulness. In contrast, individuals diagnosed withASD may encounter challenges in effectively coordinating their internal and external environments, resulting in subsequent disruptions to rhythm and temporal processes. These disruptions can have wide-ranging implications, encompassing areas such as social engagement and circadian rhythms. Individuals with ASD may exhibit disruptions in their circadian rhythms as a result of their inability to

synchronize their internal biological clock with external environmental and social cues [46-51].A range of over-the-counter formulations of melatonin is available, with doses ranging from 1 to 10 mg with a commonlyrecommended dosage of 1–3 mg approximately 30–60 minutes prior to the intended time of sleep initiation, though the dosage may vary for every individualIA recommended administration of a smaller dosage (0.5-1 mg) at an earlier time (3-4 hours before bedtime) if a circadian rhythm disorder is identified [56-59]. The efficacy of a dose is not influenced by an individual's age or weight. Melatonin is a hormone produced by the pineal gland that regulates the circadian rhythm of the body. The efficacy of melatonin in lowering sleep onset latency is evident, but, its usefulness in mitigating nocturnal awakenings and other disturbances in sleep patterns exhibits variability. In a study with a sample of 24 children diagnosed with ASD between the age range of 1 to 3 years revealed that the participants demonstrated a reduction in the time it took them to fall asleep, as measured by actigraphy, when administered either a 1 mg or 3 mg dosage. The intervention demonstrated significant enhancements in both the sleep patterns of the children as well as their behavior and the levels of stress experienced by their parents [52-55].

7.4. **Antipsychotic Medication:** There is limited tolerability and efficacy data available for the use of antipsychotic medication class in the treatment of insomnia among pediatric patients. Several studies examining the impact on sleep architecture have reported that ziprasidone, olanzapine, and risperidone have the effect of increasing slow-wave sleep. Notably, both ziprasidone and risperidone have been found to decrease REM sleep. Risperidone and olanzapine are two atypical antipsychotic medications that have been suggested as potential treatments for sleep disturbances in pediatric patients. These drugs are utilized off-label for the management of insomnia, and it is not recommended to routinely prescribe them for this purpose, especially as a primary pharmacotherapeutic intervention. The Canadian Academy of Child and Adolescent Psychiatry issued guidance recommending against the initial use of these medications for the treatment of insomnia in individuals across several age groups, including children, adults, and the elderly. Similarly, several nations have also made efforts to restrict the quantity of prescriptions permitted under government-subsidized programs [56-61].

7.5. **Antidepressant**: The available information regarding the utilization and efficacy of sedative antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs), in addressing sleep disorders among children with ASD is limited. The potential efficacy of these drugs may be observed in cases where insomnia is accompanied by concurrent psychiatric conditions. The administration of sedative antidepressants such as trazodone and mirtazapine may be advantageous for children who have comorbid depression. These pharmacological agents exert their therapeutic effects on sleep by modulating the activity of neurotransmitters associated with wakefulness, such as acetylcholine, histamine, noradrenaline, and serotonin. A notable consequence of these drugs is their tendency to diminish REM sleep and extend periods of daytime sleepiness. Trazodone is commonly selected and utilized in the field of psychiatry. The efficacy of this intervention has predominantly been demonstrated in individuals diagnosed with psychiatric disorders. The administration of Trazodone is associated with a discernible residual impact in the morning, which can be attributed to its antagonistic activity on the 5-HT2A/C receptors and its potent sedating properties as an antidepressant. There is an association between fluoxetine and the occurrence of sleeplessness. In comparison to the dosages used for the treatment of mood disorders, dosages administered for the management of insomnia are generally of a lesser magnitude [62-67].

7.6. **Alpha-AdrenergicAgonist:** The two main alpha agonists that are widely used off-label to treat autism-related sleep disturbances are clonidine and guanfacine. The administration of clonidine within a dosage range of 0.05-0.225 mg per day yielded reductions in sleep onset and maintenance difficulties experienced by children and adolescents (aged 4-16 years) diagnosed with autism and neurodevelopmental disorders. This treatment approach shown favorable tolerability and minimal occurrence of adverse effects. Some potential adverse effects of clonidine include hypotension, irritability, bradycardia, dry mouth, and suppression of REM sleep. Abrupt discontinuation of clonidine may lead to rebound hypertension and rebound REM sleep [68-70].

7.7. **Sedative and Hypnotics Drugs:**Benzodiazepines (BZDs), which are classified as hypnotics and sedatives, are commonly prescribed to adult patients experiencing insomnia. As a result of the adverse effects associated with benzodiazepines, such as

somnolence, cephalalgia, cognitive dysfunction, vertigo, and the development of tolerance and withdrawal symptoms, these medications are less usually prescribed for pediatric patients. The use of clonazepam, an intermediate-acting benzodiazepine (BZD), has been observed to yield positive outcomes in children diagnosed with developmental impairments who exhibit symptoms of partial arousals, parasomnias, periodic limb movement disorder, and nocturnal biting [71-73].

7.8. **Other Medications:** Several medications which are used in the treatment of the Alzheimer's disease are also found to be effective in the management of ASD symptoms. Drugs such as donepezil and rivastigmine are cholinesterase inhibitors that increase the acetylcholine by preventing its destruction. ASD is associated with anomalies in the cholinergic system that was discovered in post-mortem brain samples from people with ASD [1, 74-76].

Conclusion:

Sleep disturbances are a common symptom of neurodevelopmental disorders, and these disturbances can have a significant impact on the lives of the individuals who experience them as well as the lives of their families. Recognizing the complexity of the relationship between sleep and a variety of disordersis vital for the development of successful treatments, as well as for boosting the general well-being and quality of life of individuals..Sleep plays a critical role in the body's natural healing process, hormonal balance, functions, and biological components. Neurodevelopmental disordersare complex conditions, it is absolutely necessary to implement a comprehensive and individualized approach to the management of sleep disturbancesto meet the requirements that are unique to each individual with and without intellectual developmental disabilities. Early detection of neurodevelopment disorders may yield promising treatment approaches to improve sleep quality and duration.

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