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Review Article

Delayed sleep phase syndrome: the sleep disorder that's out of sync

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ABSTRACT

Delayed sleep phase syndrome (DSPS) is a chronic sleep disorder marked by a persistent delay in the sleep-wake cycle, causing individuals to fall asleep and wake up much later than desired. It affects people of all ages but is especially common in teenagers and young adults. DSPS significantly disrupts daily functioning, leading to mood swings, cognitive impairment, daytime sleepiness, and social or occupational difficulties. The disorder's pathophysiology is complex, involving circadian rhythm misalignment, melatonin secretion irregularities, and sleep-wake imbalances. Genetic predisposition, environmental influences, and lifestyle choices can increase susceptibility and perpetuate the condition. Clinically, DSPS is characterized by late sleep onset, late rising, and a strong preference for a delayed sleep schedule. Associated traits include erratic melatonin levels, inconsistent sleep patterns, and circadian rhythm disturbances. Diagnosis requires a thorough clinical evaluation, including sleep diaries, actigraphy, polysomnography (PSG), and a detailed history. Differentiating DSPS from conditions such as insomnia, narcolepsy, or sleep apnoea is essential to avoid mismanagement. Treatment typically combines behavioral, environmental, and pharmacological strategies. Behavioral approaches include consistent sleep routines, relaxation methods, and cognitive behavioral therapy. Environmental interventions involve light therapy, sleep hygiene improvements, and melatonin supplementation. Pharmacological options may include melatonin receptor agonists, sleep-promoting agents, or wakefulness-enhancing medications. Early recognition and treatment are vital to preventing long-term impairment and improving quality of life. Raising awareness among patients, families, and healthcare professionals is crucial. This study emphasizes bridging clinical practice and research, while providing a valuable resource for students, clinicians, and investigators in sleep medicine.

Keywords: Pathophysiology, Diagnosis, Treatment options, Sleep medicine, Neuroscience, Circadian rhythm disorder, Sleep phase shift, Sleep-wake cycle, Daytime sleepiness, Sleep quality

INTRODUCTION

Sleep is a vital component of both physical and mental restoration in humans. The sleep-wake cycle, which is regulated by intricate system involving suprachiasmatic nucleus (SCN), melatonin, and other neurotransmitters, typically follows a circadian rhythm. However, in some individuals, this natural rhythm is disrupted, leading to sleep disorders that can significantly impact daily life.[1]

DSPS is a common sleep disorder that affects millions of people worldwide. Despite its prevalence, DSPS remains poorly understood, and its diagnosis is often delayed or missed. This review aims to provide a comprehensive overview of DSPS, including its definition, epidemiology, pathophysiology, symptoms, diagnosis, and treatment options. The paper also highlights the significance of DSPS, its impact on daily life, and the need for early recognition and intervention.

DSPS, a chronic condition characterized by a persistent delay in the sleep-wake cycle, is an example of this type of sleep disturbance. According to, this delay results in later sleep and wake-up times, which frequently lead to severe distress and functional impairment in social, occupational, and other domains.[2]

In complex sleep conditions, DSPS is caused by a confluence of behavioural, environmental, and hereditary variables. Although people of all ages can be affected by illness, teenagers and young adults are disproportionately afflicted. An estimated 7-16% of adolescents and young adults are affected by DSPS, with a higher frequency among males.[3] The consequences of untreated DSPS can be severe, leading to impaired cognitive function, mood disturbances, and an increased risk of sleep-related problems, such as sleep apnoea and insomnia.[4]

Furthermore, DSPS can have a significant impact on daily life, causing difficulties in maintaining relationships, work, or school/college obligations

Despite its prevalence and significant consequences, DSPS remains poorly understood, and its diagnosis is often delayed or missed.

A comprehensive understanding of DSPS, including its pathophysiology, clinical features, diagnosis, and treatment options, is essential for developing effective management strategies and improving the quality of life of affected individuals with this condition.[1]

DSPS has evolved. The following is a brief timeline:

Early beginnings

1672

First recorded description of a sleep disorder resembling DSPS was made by Swiss physician Thomas Willis.[1]

19th century

Various reports of "nocturnal habits" and "eveningness" have appeared in the medical literature.[3]

Development of modern concepts

1950s-1960s

Researchers like Nathaniel Kleitman and William C. Dement began studying sleep patterns and circadian rhythms.

1970s-1980s

The concept of DSPS started taking shape, with reports of "DSPS " and "circadian rhythm sleep disorders."

Formal recognition

1981

The American sleep disorders association (ASDA) officially recognized DSPS as a distinct sleep disorder.

1990

The international classification of sleep disorders (ICSD) first included DSPS as a diagnostic category.

2005

The ICSD-2 further refined the diagnostic criteria for DSPS.

2014

The ICSD-3 provided updated criteria and classifications for DSPS.

ONGOING RESEARCH AND UPDATES

Genetics and molecular mechanisms

Circadian rhythm regulation

Studies have shown that DSPS is linked to alterations in the body's internal clock, which regulates various physiological processes. The SCN, the master biological clock, plays a crucial role in synchronizing the body's circadian rhythms with external light-dark cycles.[5]

Genetic studies

Researchers have investigateded genetic variants associated with DSPS**,** such as PER3 and CLOCK polymorphisms.[4]

Diagnostic and assessment tools

Actigraphy and wearable devices

Researchers are developing and validating actigraphy-based methods for assessing sleep patterns and circadian rhythms in DSPS.[6]

Sleep diaries and mobile apps

Studies have investigated the use of sleep diaries and mobile apps to monitor sleep patterns and symptoms in DSPS.[4]

Treatment and intervention strategies

Cognitive-behavioural therapy for insomnia (CBT-I)

Studies have investigated the effectiveness of CBT-I in addressing insomnia symptoms in DSPS.[7]

Light therapy and melatonin

Researchers are currently examining the efficacy of light therapy and melatonin supplementation for treating DSPS.[21]

Physical activity and exercise

Researchers are exploring the impact of physical activity and exercise on sleep patterns and symptoms in the DSPS.[24]

Neuroimaging and neurophysiological studies

Electroencephalography (EEG) and PSG

Researchers have used EEG and PSG to examine sleep stage transitions, sleep spindles, and other neurophysiological markers in DSPS.[4]

Functional magnetic resonance imaging (fMRI)

Studies have used fMRI to investigate changes in brain activity and connectivity during DSPS.[3]

EPIDEMIOLOGY AND COMORBIDITIES

Cognitive impairments

Executive functioning deficits negatively impacting daily life and productivity (ICSD-3).

Physical health complications

Metabolic disturbances, cardiovascular risk, and gastrointestinal issues.

Comorbid mental health conditions

Depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD). Studies suggest that individuals with ADHD are more prone to DSPS due to shared underlying circadian rhythm differences. DSPS can exacerbate ADHD symptoms, making accurate diagnosis and treatment crucial.[8]

These ongoing research efforts aim to improve our understanding of DSPS, develop more effective treatments, and enhance the quality of life of individuals with this condition.[3]

Current research continues to advance our understanding of DSPS, its causes, and its effective treatments.[1]

THE IMPORTANCE OF SLEEP

Emotional control

Sleep helps regulate emotions by allowing the brain to process and consolidate emotional experiences. REM sleep is thought to play a role in emotional regulation, with studies showing that it helps reduce emotional reactivity. Research suggests that sleep deprivation can lead to increased negative emotions and decreased positive emotions.

In infants, sleep state transitions (e.g., quiet sleep and wakefulness) have been linked to better emotional development.[9]

Brain development

Sleep is essential for learning and memory consolidation, with NREM sleep and REM sleep playing distinct roles in this process.

Sleep helps stimulate creative thinking and problem-solving skills.

In children, sleep has been linked to improved cognitive development, including better performance in working memory tasks.

Adequate sleep is also important for brain structure development, with research suggesting that sleep affects the development of neural circuits.[10]

Cardiovascular health

Long-term sleep deprivation increases the risk of heart attacks, strokes, and high blood pressure, among other cardiovascular diseases.[1]

Physical restoration

Sleep enables our bodies to develop muscles and bones, improve our immune systems, and repairs and regenerate tissues.[25]

Cognitive function

Learning, memory consolidation, and attention depend on sleep.[21]

SIGNIFICANCE OF SLEEP FOR LIVING BEINGS

Predator avoidance

Certain species sleep during the day and are active at night, which helps them evade predators.[1]

Mating and reproduction

In certain animals, sleep influences hormones and behaviors involved in reproduction.[7]

Immune function

The immune systems of animals depend on sleep to prevent illnesses and infections.[6]

Evolutionary conservation

From fruit flies to humans, sleep is a fundamental component of life that is preserved across species.[25]

Conserving energy

Sleep lowers metabolic rates and energy expenditure, helping animals conserve energy.[26]

Some common sleep disorders that affect human beings are as follows.

PRIMARY SLEEP DISORDERS

Restless leg syndrome (RLS), also known as Willis-Ekbom disease, is a neurological disorder characterized by unpleasant sensations in the legs and an irresistible urge to move them, often disrupting sleep. RLS can be primary or secondary to conditions like iron deficiency, end-stage renal disease, and pregnancy.[28]

Conditions that mimic RLS

Nighttime leg cramps

Painful cramps in the calf or soles of the feet, often short-lived and not indicative of RLS.

Anxiety disorders

Can cause restlessness and agitation at night, like RLS symptoms.

Peripheral neuropathies

Disorders of the nerves causing burning, tingling, and shooting sensations in limbs, not relieved by movement.

Akathisia

A state of restlessness or agitation, often caused by certain medications.

Meralgia paresthetica

A rare nerve disorder causing numbness, pain, burning, and tingling in the thigh.[28]

Sleep apnea

Pauses in breathing during sleep.[1]

Insomnia

Difficulty falling or staying asleep.[4]

Periodic limb movement disorder (PLMD)

Repetitive limb movements during sleep.[4]

Narcolepsy

Excessive daytime sleepiness and sudden sleep attacks.[3]

Circadian rhythm sleep disorders

Advanced sleep phase disorder

The sleep schedule advances beyond normal hours.[2]

Shift work sleep disorder

Sleep disruption due to non-traditional work schedules.[7]

DSPS

Sleep schedule is delayed beyond normal hours.[3]

Jet lag disorder

Sleep disruption due to travel across time zones.[21]

Parasomnias

Night terrors (Sleep terrors)

Episodes of intense fear, anxiety/panic, typically occurring during deep sleep. Individuals may scream, thrash/become violent, often with no memory of event.[29]

Sleepwalking (Somnambulism)

Walking or performing complex behaviors during sleep.[25]

Sleep eating disorder

Eating during sleep.[26]

Sleep talking (Somniloquy)

Talking during sleep.[3]

Other sleep disorders

Sleep-related movement disorders

Disorders that cause abnormal movements during sleep.[1]

Bruxism

Grinding or clenching teeth during sleep.[7]

Sleep-related eating disorder

It is often accompanied by other sleep disorders.[4]

THE CAUSES/ ETIOLOGY OF DSPS

Internal factors

Melatonin regulation

Melatonin levels: Research suggests that individuals with DSPS often have altered melatonin secretion patterns,

with delayed peak melatonin levels. This can contribute to the delayed sleep phase.

Melatonin suppression: Exposure to light in the evening can suppress melatonin production, making it harder to fall asleep.[11]

Sleep-wake homeostasis

Sleep pressure: Build-up of sleep pressure/drive to sleep, is regulated by sleep-wake homeostasis. In DSPS this process may be leading to delayed sleep timing.[12]

Circadian rhythm regulation

Circadian clock: The internal circadian clock regulates the body's natural sleep-wake cycle. In DSPS, the circadian clock may be delayed, leading to a mismatch between the body's natural sleep-wake cycle and external environmental cues.[1]

Genetic predisposition

Family history of DSPS or other sleep disorders.[3]

External factors

Environmental factors

Noise, temperature, and other environmental disruptions that affect sleep.[7]

Lifestyle habits

Irregular sleep schedules, staying up late, or working during non-traditional hours.[2]

Social and cultural influences

Social pressures to stay up late or conform to unconventional sleep schedules.[3]

Light exposure

Prolonged exposure to screens (e.g., smartphones, tablets, or computers) before bedtime.[21]

Medical factors

DSPS can significantly impact chronic pain and sleep disorders due to the complex interplay between sleep regulation, pain perception.

Sleep disturbances in chronic pain

Sleep quality

Poor sleep quality is common in chronic pain patients, with reduced sleep efficiency, altered sleep architecture, and increased sleep fragmentation.

Pain intensity

Sleep disturbances can exacerbate pain intensity, while improved sleep quality can reduce pain severity.[13]

Psychological factors

Mental health disorders

Depression, anxiety, and other psychiatric conditions that disrupt sleep.[4]

Neurological disorders

Parkinson's disease, multiple sclerosis, and other conditions that affect sleep regulation.[26]

Developmental factors

Aging

Changes in sleep patterns and circadian rhythm regulation with age.[4]

Adolescence

Natural shift in the sleep-wake cycle during puberty.[3]

THE CLINICAL FEATURES OF DSPS

Primary symptoms

Insistence on maintaining the delayed sleep schedule

Individuals with DSPS often find it challenging to adjust their sleep schedule to an earlier time frame.[30]

Delayed sleep onset

Difficulty falling asleep until late at night/early morning.[4]

Delayed wake-up time

Sleeping late, often until afternoon.[3]

Secondary symptoms

Daytime sleepiness

Excessive sleepiness during the day, which can lead to difficulties in school/college, work, or social settings.[14]

Increased risk of sleep-related problems

Sleep apnoea, insomnia, or other sleep disorders.[1]

Impaired cognitive function

Difficulty concentrating, memory lapses, decreased productivity.[7]

Mood disturbances

Irritability, anxiety, and depression are the mood disturbers.[2]

Social and occupational dysfunction

Difficulty maintaining relationships, work, or school/college obligations due to delayed sleep schedule.[21]

Associated features

Melatonin level abnormalities

Individuals with DSPS tend to have delayed melatonin production, which starts and ends later than normal. This delay makes it difficult for them to fall asleep at conventional times. Melatonin production is typically high during the night and low during the day, but in DSPS, this rhythm is shifted later.[1]

Circadian rhythm abnormalities

The internal body clock, regulated by the SCN, is disrupted in DSPS. The SCN generates circadian rhythms through feedback loops of transcription and translation. Lesions in the SCN can abolish melatonin rhythm, demonstrating its crucial role in regulating circadian rhythmicity.[15]

Light exposure and melatonin suppression

Bright light exposure, especially blue light from electronic devices, can suppress melatonin production and further delay circadian rhythm. Conversely, morning light exposure can help regulate the internal clock.[16]

Sleep-wake cycle irregularities

Unpredictable sleep patterns, including sleep phase shifts.[3]

Age-specific features

Young adults

Prevalence: Approximately 7-16% of adolescents and young adults are affected by DSPS, with some studies suggesting that up to 15% of this population may experience the condition.

Delayed sleep onset: Young adults with DSPS tend to fall asleep significantly later than desired, often after midnight, leading to difficulties waking up in morning.

Difficulty waking up: Individuals with DSPS struggle to wake up at conventional times, resulting in impaired daily functioning, social, and occupational difficulties.

Sleep quality: Despite the delayed sleep phase, young adults with DSPS often sleep well in terms of duration and quality once they fall asleep.

Impact on daily life: DSPS can significantly interfere with work, school/college, and social life due to the mismatch between the individual's sleep-wake cycle and societal norms.[31]

Older adults: Sleep patterns may become more irregular with age.[4]

Adolescents: The delayed sleep phase often begins during puberty.[3]

THE DIAGNOSIS PROCESS FOR DSPS

Diagnostic criteria

The ICSD and the American academy of sleep medicine (AASM) offer the following diagnostic standards for DSPS.

Delayed sleep schedule

Wake-up and sleep timings are regularly later than preferred or considered socially acceptable.[1]

Sleep length is normal, and the amount of time spent sleeping falls within a typical range.[7]

Persistent symptoms

The symptoms last for a minimum of three months.[2]

Sleep quality is normal

After sleep starts, sleep quality is normal.[25]

Stable sleep-wake cycle

The delayed sleep-wake cycle is stable, with a regular sleep schedule.[17]

TOOLS FOR DIAGNOSIS

DSPS can be verified using the diagnostic tools listed below:

Circadian phase markers

Such as core body temperature and cortisol levels, can help assess the timing of the internal clock.[17]

PSG

PSG is an overnight sleep study that records various physiological activities, such as brain waves, muscle activity, and heart rate. While PSG is not typically used to

diagnose DSPS, it can help rule out other sleep disorders.[29]

PSG can provide information on sleep stages, sleep quality, and potential sleep disruptions.

Melatonin level measurement

Measuring melatonin levels can help assess the timing of the endogenous circadian pacemaker. Dim light melatonin onset (DLMO) is a commonly used measure to evaluate melatonin levels.[18]

Sleep diary

A record or sleep diary is used to monitor sleep patterns, such as the period of wakefulness, the start of sleep, and the quality of sleep.[1]

Actigraphy

It is a wearable technology that monitors sleep and activity patterns.[2]

Physical examination

To rule out underlying medical issues, a physical examination is conducted.[3]

Differential diagnosis

The following circumstances should be considered when making a differential diagnosis for DSPS.

Insomnia

A sleep condition marked by trouble getting to sleep or remaining asleep.[7]

Sleep apnoea

A condition that causes breathing pauses while you are asleep.[1]

Circadian rhythm disorder

A disorder characterized by disruption in the body's natural sleep-wake cycle.[4]

Narcolepsy is a neurological condition characterised by excessive drowsiness during day.[3]

THE TREATMENT OF DSPS

The treatment of DSPS typically involves a multidisciplinary approach that incorporates behavioral, environmental, and pharmacological interventions. The primary goal of treatment is to realign the sleep-wake cycle with the desired sleep schedule, improve sleep quality, and reduce the symptoms of daytime sleepiness and fatigue.

Behavioral interventions

Sleep hygiene

Establishing good sleep hygiene practices, such as avoiding caffeine, nicotine, and electronic devices before bedtime.[1]

Sleep schedule regularization

Establishing a consistent sleep schedule, with a gradual adjustment to the desired sleep-wake cycle.[6]

Relaxation techniques

Practicing relaxation techniques, such as progressive muscle relaxation, deep breathing, or meditation, to reduce stress and anxiety.[21]

Cognitive-behavioral therapy (CBT)

Identifying and changing negative sleep habits and thoughts, promoting a healthier sleep-wake cycle.[22]

Environmental interventions

Melatonin supplementation

Taking the correct dosage of melatonin supplements at the correct timing can help the regulate sleep-wake cycles. Typical dosages range from 0.5 to 5 mg, taken 30 minutes to 2 hours before bedtime.[19]

Sleep environment optimization

Creating a sleep-conducive environment, such as a dark, quiet, or cool room, to promote better sleep.[25]

Light therapy

Exposure to bright light, particularly in the morning, helps regulate circadian rhythms.[3]

Pharmacological interventions

Melatonin receptor agonists

Suggested medications like ramelteon or tasimelteon, which target melatonin receptors to regulate sleep-wake cycles.[7]

Sleep-promoting medications

Medications like sedatives or hypnotics, used under medical guidance, to promote sleep.[2]

Wake-promoting medications

Found that medications like modafinil or armodafinil, used under medical guidance, promote wakefulness.[6]

Alternative therapies

Chronotherapy

This involves systematically adjusting sleep schedules to align with desired sleep-wake times. A personalized plan developed with healthcare providers can help individuals with DSPS gradually shift their sleep times.[20]

Physical activity

Researchers like emphasized that regular physical activity, especially in the morning, can help regulate the circadian rhythm.[22]

Mindfulness-based interventions

Mindfulness-based stress reduction (MBSR) or mindfulness-based cognitive therapy (MBCT) can help reduce stress and anxiety.[23]

Lifestyle modifications

Establishing a relaxing bedtime routine

Suggested engaging in relaxing activities, like reading or meditation, before bedtime.[4]

Getting morning sunlight exposure

Exposure to natural sunlight in the morning helps regulate the circadian rhythm.[3]

Avoiding electronic gadgets

Avoid looking at bright screens beginning two to three hours before bed. Protect oneself from blue light at night.[27]

It is essential to work with healthcare professionals to develop personalized treatment plans, as individual responses to treatment may vary.

CONCLUSION

DSPS is a complex and multifaceted sleep disorder that affects individuals of all ages, with significant consequences on daily life. The condition is characterized by a persistent delay in the sleep-wake cycle, resulting in late sleep onset and late wake-up times.

The pathophysiology of DSPS involves a combination of genetic, environmental, and lifestyle factors, including abnormalities in the body's natural sleep-wake cycle, melatonin regulation, and sleep-wake homeostasis. A comprehensive understanding of these factors is essential for developing effective management strategies.

The clinical features of DSPS include delayed sleep onset, delayed wake-up time, and insistence on maintaining the delayed sleep schedule. Secondary symptoms may include daytime sleepiness, impaired cognitive function, mood disturbances, and social and occupational dysfunction.

Diagnosis of DSPS is based on a comprehensive sleep history, sleep diary, actigraphy, and PSG. Differential diagnosis should consider other sleep disorders, such as sleep apnoea, insomnia, and narcolepsy.

Treatment of DSPS typically involves a multidisciplinary approach, incorporating behavioural, environmental, and pharmacological interventions. The primary goal of treatment is to realign the sleep-wake cycle with the desired sleep schedule, improving sleep quality, and reducing symptoms of daytime sleepiness and fatigue.

In conclusion, DSPS is a complex sleep disorder that requires a comprehensive understanding of its pathophysiology, clinical features, diagnosis, and treatment options. Early recognition and treatment of DSPS are essential to prevent long-term consequences and improve quality of life.

Increased awareness and education among healthcare professionals, patients, and families are necessary to promote timely diagnosis and effective management of this complex sleep disorder. Future research should focus on developing more effective treatment strategies, exploring the underlying causes of DSPS, and improving our understanding of the complex interactions between genetic, environmental, and lifestyle factors.

By working together, we can improve the lives of individuals affected by DSPS and promote better sleep health for all.

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