

Interplay Between Obstructive Sleep Apnea and Depression: A Comprehensive Review

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Abstract

Obstructive Sleep Apnea (OSA) is a common sleep disorder with the prevalence 2-5% of the general middle-aged population and approximately half of the people worldwide have OSA. This condition is prevalent, affecting millions of people worldwide, and is associated with several risk factors, including obesity, age, and family history. Depression, on the other hand, is a serious mental condition marked by persistent feelings of low mood and anhedonia and guilt feelings. It also presented with hopelessness, helpless fleeing with lack of interest and pleasure in doing daily activities. Recent research has highlighted a significant connection between OSA and depression, suggesting that these two conditions often coexist and may exacerbate each other. Obstructive Sleep Apnea (OSA) and depression are two prevalent serious health conditions that often coexist, creating a complex interplay of symptoms that can complicate diagnosis and treatment of both conditions.

Key Words: obstructive sleep apnea (OSA); depression; obesity; anhedonia; hypercapnia; guilt feelings; hormonal and psychosocial factors; CPAP sleep disturbances; Orexin's impact neurotransmitters; serotonin; dopamine; norepinephrine

Introduction

Obstructive Sleep Apnea (OSA) is a common sleep disorder with the prevalence 2-5% of the general middle-aged population and approximately half of the people worldwide have OSA. This condition is prevalent, affecting millions of people worldwide, and is associated with several risk factors, including obesity, age, and family history. Depression, on the other hand, is a serious mental condition marked by persistent feelings of low mood and anhedonia and guilt feelings. It also presented with hopelessness, helpless fleeing with lack of interest and pleasure in doing daily activities. Recent research has highlighted a significant connection between OSA and depression, suggesting that these two conditions often coexist and may exacerbate each other. Obstructive Sleep Apnea (OSA) and depression are two prevalent serious health conditions that often coexist, creating a complex interplay of symptoms that can complicate diagnosis and treatment of both conditions. Understanding the overlap between these conditions is crucial for effective management and improved patient outcomes. It's essential to recognize that the relationship between OSA and depression is complex, and overlapping symptoms can contribute to misclassification and poor prognosis.

Obstructive Sleep Apnea (OSA) vs Depression symptoms:

OSA according to ICS ver. 3 is a sleep disorder characterized by repeated episodes of partial or complete obstruction of the upper airway during sleep. This leads to disrupted sleep and reduced oxygen levels in the blood. OSA occurs when the muscles at the back of the throat fail to keep the airway open, despite efforts to breathe. This can result in loud snoring,

choking, or gasping sounds during sleep, and excessive daytime sleepiness. OSA has common symptoms such as loud snoring sounds with episodes of breathing cessation during sleep. It also presented with abrupt awakenings patterns accompanied by gasping or choking. There are morning headaches with excessive daytime sleepiness, and difficulty in concentration with irritable mood. Depression on the other hand, according to DSM V is a mood disorder that affects how a person feels, thinks, and behave that leads to daily activities impairment. It is marked by persistent feelings of sadness and a lack of interest or pleasure in previously enjoyed activities. There are common symptoms of depression that include: Persistent low, sad anxiety, or "empty" mood, feelings of hopelessness, helplessness, uselessness and pessimism. Also, there is Irritability, Loss of interest in hobbies and activities with fatigue and decreased energy and cognitive function. There are difficulties in concentration, attention and making decisions. Also, there are Insomnia, or hypersomnia with increased appetite or weight loss.

The overlapping symptoms between OSA and Depression:

Several symptoms of OSA and depression overlap, making it challenging to distinguish between those two conditions. There is fatigue and excessive daytime sleepiness. In OSA, this is due to disrupted sleep pattern and poor sleep quality. In depression, fatigue is often a result of the mental and emotional strain associated with the condition.

Also, there are Irritability and Individuals with OSA may experience irritability due to sleep deprivation and the physical strain of interrupted breathing. Similarly, irritability is a common symptom of depression,

often linked to feelings of frustration and helplessness. Difficulty Concentrating and Cognitive impairment, including difficulty concentrating and memory problems, are symptoms shared by both OSA and depression. In OSA, this is often due to the lack of restorative sleep, while in depression, it is related to the overall impact of the disorder on brain function. As mentioned earlier, both conditions can cause significant sleep disturbances. OSA leads to frequent awakenings due to breathing interruptions, while depression can cause insomnia or hypersomnia (excessive daytime sleepiness). Morning headaches are common in individuals with OSA due to oxygen deprivation during sleep. While depression can also cause headaches, often linked to stress and tension.

The Interplay Between OSA and Depression

Research indicates a bidirectional relationship between OSA and depression. OSA can contribute to the development of depressive symptoms due to chronic sleep disruption and the resulting impact on overall health and well-being. Conversely, depression can exacerbate the symptoms of OSA by affecting sleep patterns and increasing the perception of fatigue and other physical symptoms. The development of depression in individuals with obstructive sleep apnea (OSA) is multifactorial and not fully understood. Depression is prevalent in people with obstructive sleep apnea (OSA), as reported by clinical studies. The clinical samples, showed the prevalence of depression in OSA patients ranges from 20% to approximately 40%. These studies often involve patients seeking medical attention for their OSA symptoms. Also, it has shown in community-based studies, the prevalence of depression in people with OSA has been reported to range from 5% to 63%². These studies include a broader population, not just those actively seeking treatment. Comparison to Non-OSA Individuals: A significantly higher prevalence of depression was identified in people with OSA (around 21.8%) compared to those without OSA (approximately 9.43%). It's essential to recognize that the relationship between OSA and depression is complex, and overlapping symptoms can contribute to misclassification. However, several mechanisms and factors contribute to this relationship. OSA leads to frequent disruptions in sleep due to repeated episodes of partial or complete airway obstruction. These disruptions affect sleep quality, leading to daytime fatigue, irritability, and mood changes. Chronic sleep deprivation can contribute to the development of depression. During apneic events, blood oxygen levels drop (hypoxia), and carbon dioxide levels rise (hypercapnia). These physiological changes can impact brain function, alter neurotransmitter levels, and contribute to mood disturbances. Also, OSA is associated with increased inflammation in the body. Chronic inflammation may affect brain function and contribute to depressive symptoms. OSA-related sleep disturbances can disrupt neurotransmitter balance, including serotonin, dopamine, and norepinephrine. These imbalances are linked to mood disorders such as depression. The impact of OSA on daily life activities, including relationships, and work can lead to stress, anxiety, and depression and coping with OSA-related challenges can be emotionally taxing. OSA and depression also share common risk factors, such as obesity, sedentary lifestyle, and metabolic syndrome. Again, these factors may contribute to both conditions are: The role of Obesity that plays a significant role in both depression and obstructive sleep apnea (OSA). Here's how they are interconnected: Obesity, particularly central obesity (excess fat around the abdomen), is a major risk factor for OSA. The excess weight (high BMI) can lead to increased fat deposits around the upper airway, which can obstruct breathing during sleep. Also, Researches have showed obesity is linked to depression. The relationship is bidirectional, meaning obesity can lead to depression and vice versa. Factors such as low self-esteem, social isolation, and inflammation are thought to contribute to this relationship. Also, the Inflammation process has a role in OSA and depression that are associated with increased levels of inflammatory cytokines, which can contribute to the development and worsening of both conditions. Age plays a significant role in both obstructive sleep apnea (OSA) and depression, influencing their

prevalence and severity. The prevalence of OSA increases with age and particularly common in older adults, with studies showing that more than 50% of individuals over the age of 65 may be affected. This is due to age-related changes in the structure and function of the upper airway, as well as an increase in other risk factors such as obesity and comorbidities. On the other hand, depression can occur at any age, but its characteristics and prevalence can vary. Younger individuals with OSA tend to have more severe depressive symptoms compared to older adults¹. In older adults, depression is often associated with chronic illnesses, including OSA, and can be exacerbated by the physical and social changes that come with aging. There is a notable overlap between OSA and depression, and age can influence this relationship. For instance, younger individuals with OSA may experience more severe depression, while older adults may have a higher prevalence of both conditions. Also, Family factors can significantly influence both depression and obstructive sleep apnea (OSA). There is genetic predisposition, which both depression and OSA can have genetic components. As mentioned, the positive family history of depression increases the likelihood of developing depressive disorders among family members. Similarly, OSA can run in families due to inherited physical traits like a narrow airway or obesity.

Family environment plays a crucial role in mental health. Stressful family dynamics, lack of support, or exposure to negative behaviors can contribute to the development of depression. For OSA, family lifestyle habits, such as diet and physical activity levels, can influence the risk of obesity, a major factor in OSA. Also, families often share health behaviors that can impact both conditions. For example, poor sleep hygiene and sedentary lifestyles can increase the risk of both depression and OSA. With supportive family environment, both conditions as mentioned above could be helped and managed. Emotional support from family members can alleviate depressive symptoms, while practical support can help in managing OSA, such as encouraging adherence to CPAP therapy and healthy life style. Gender also plays a significant role in both depression and anxiety, influencing their prevalence, symptoms, and treatment outcomes. Women are generally more susceptible to both depression and anxiety disorders compared to men. Studies show that women are about twice as likely to experience these conditions. This higher prevalence is thought to be due to a combination of biological, hormonal, and psychosocial factors. Although, the symptoms of depression and anxiety can manifest differently between genders, Women often report more internalizing symptoms, such as sadness, guilt, and anxiety, while men may exhibit more externalizing behaviors, such as irritability, anger, and substance abuse.

Hormonal fluctuations, particularly those related to the menstrual cycle, pregnancy, and menopause, can contribute to the higher rates of depression and anxiety in women. These hormonal changes can affect mood and stress levels, making women more vulnerable to these conditions. Regarding the social and cultural Factors, it was reported that Gender roles and societal expectations can also play a role. Women often face higher levels of stress related to caregiving responsibilities, work-life balance, and social pressures, which can increase their risk of developing depression and anxiety. Within treatment response, there are also gender differences in how individuals respond to treatment. Women generally have better access to mental health services and may respond more positively to certain treatments, although more research is needed to fully understand these differences. Addressing the subject from a different angle, the role of Thyroid hormones which have been playing a significant role in both depression and obstructive sleep apnea (OSA). In Depression, Hypothyroidism which means Low levels of thyroid hormones, TSH, T4(hypothyroidism) are commonly associated with depression. Symptoms of hypothyroidism, such as fatigue, weight gain, and cognitive impairment, can overlap with depressive symptoms. Additionally, hypothyroidism can lead to changes in brain chemistry that affect mood to become low. So thyroid hormone treatments can enhance the effectiveness of antidepressants, suggesting a close link between thyroid function and mood regulation. Also, Hypothyroidism may contribute to

the development of OSA. The mechanisms include increased mucopolysaccharide and protein deposition in the upper airway, which can lead to airway obstruction. Additionally, hypothyroidism can affect the regulatory control of pharyngeal dilator muscles, further contributing to OSA. Also, Hypothyroidism can depress respiratory centers in the brain, leading to reduced respiratory drive and increased risk of sleep apnea.

Illicit substances substance such as Alcohol can significantly impact both depression and obstructive sleep apnea (OSA), often worsening the symptoms of each condition. Initially alcohol might seem to improve mood, it ultimately exacerbates depression. It can interfere with the effectiveness of antidepressant medications, making symptoms harder to manage. People with depression may use alcohol to self-medicate, but this often leads to a vicious cycle where alcohol use worsens depressive symptoms. On the other hand, Alcohol relaxes the muscles in the throat, increasing the likelihood of airway obstruction during sleep. This can worsen OSA by making apneas (pauses in breathing) more frequent and severe. Also, Alcohol disrupts normal sleep patterns, leading to poorer sleep quality and more fragmented sleep, which can exacerbate OSA symptoms. To sum up, there are a Combined Effects and a clear Bidirectional Relationship. Both depression and OSA can lead to increased alcohol use as individuals may try to cope with their symptoms. However, this often results in a cycle where alcohol use worsens both conditions. Managing these conditions becomes more challenging when alcohol use is involved. It's crucial to address alcohol use as part of a comprehensive treatment plan for both depression and OSA.

The Role of Orexin in the interplay:

There is a clear role for orexin in both conditions, emphasizing the focus on orexin and its implications in depression and OSA, suggesting an exploration of both. Orexins are neuropeptides produced in the lateral hypothalamus that are involved in various functions, including sleep, arousal, and mood regulation. Orexin neurons connect to brain regions involved in mood regulation, such as the hippocampus, enhancing neurogenesis and improving mood, while orexin deficiency can lead to mood disorders like depression. Additionally, dysregulation of orexin signaling has been linked to conditions such as anxiety, panic disorder, depression and addiction. Also, there are Orexin's role in maintaining wakefulness and muscle tone could influence the stability of the upper airway during sleep, potentially contributing to OSA.

The underlying mechanisms Of Orexin:

As mentioned before, Orexin, a neuropeptide produced in the hypothalamus, plays a significant role in regulating sleep-wake cycles and arousal. While its primary function is to promote wakefulness and inhibit REM sleep, recent research suggests that orexin might also be involved in the development of obstructive sleep apnea (OSA). OSA is a medical condition characterized by repeated episodes of partial or complete obstruction of the upper airway during sleep, leading to disrupted sleep and reduced oxygen levels. Orexin's role in maintaining wakefulness and muscle tone could influence the stability of the upper airway during sleep, potentially contributing to OSA. Understanding the exact mechanisms by which orexin affects OSA is still an ongoing area of research, but it highlights the complex interplay between neuropeptides and sleep disorders. Here are some keyways how orexin affects OSA. Orexin increases the activity of upper airway dilator muscles, which helps keep the airway open during sleep. This is particularly important in preventing the collapse of the airway, a hallmark of OSA. Studies on respiratory function have shown that orexin receptor antagonists, such as suvorexant, do not significantly impair respiratory function in patients with mild to moderate OSA. These medications can improve sleep quality without worsening OSA symptoms. As we know, orexin is crucial for maintaining wakefulness, stabilizing and regulating sleep-wake cycles. Disruptions in orexin signaling can lead to fragmented sleep, which is often seen in OSA patients. Orexin also influences autonomic functions, including

cardiovascular regulation that can be particularly relevant in OSA, where disrupted sleep can lead to cardiovascular issues.

These mechanisms highlight the complex role of orexin in both the pathophysiology and potential treatment of OSA. Some antidepressant medications can affect orexin levels and it have shown that the selective serotonin reuptake inhibitor (SSRI) such as sertraline can slightly reduce orexin-A levels after several weeks of treatment. Additionally, there is ongoing research into the use of orexin receptor antagonists as potential treatments for depression. These medications, which block the action of orexin, have shown some promise in pre-clinical studies. Orexin, also known as hypocretin, plays a significant role in regulating sleep, appetite, and the stress response. Its dysfunction has been linked to depression. Recent studies have explored the potential of orexin receptor antagonists (ORAs) as treatments for depression. These compounds, initially developed for insomnia, have shown some promise in pre-clinical and clinical trials. For example, dual orexin receptor antagonists (DORAs) like almoxerant have demonstrated antidepressant-like effects in rodent models¹. However, the evidence from selective orexin receptor antagonists (ORAs) is still conflicting. Also, Orexin does play a significant role in regulating mood. Orexins are neuropeptides produced in the hypothalamus and are involved in various functions, including sleep, arousal, and mood regulation [12]. Orexin neurons connect to brain regions involved in mood regulation, such as the hippocampus [3]. They enhance neurogenesis and improve mood, while orexin deficiency can lead to mood disorders like depression [3]. Additionally, dysregulation of orexin signaling has been linked to conditions such as anxiety, panic disorder, and addiction. Orexins may be involved in the development of low mood and depression. As we know, disrupted sleep in OSA due to frequent apneic events affects orexin levels that regulate sleep wake cycle, leading to daytime sleepiness and fatigue. Similarly, sleep disturbances contribute to mood changes in depression.

Secondly, Orexin's impact neurotransmitters like serotonin, dopamine, and norepinephrine. Imbalances in these neurotransmitters are associated with both OSA symptoms and depressive states. Finally, Orexins modulate the body's stress response and ongoing chronic stress can contribute to depression, and OSA-related stressors may exacerbate mood disturbances. OSA and depression share common risk factors (e.g., obesity), suggesting interconnected pathways that exist. Let's explore how orexins may be involved in the development of obstructive sleep apnea (OSA). As mentioned above, Orexins has a primarily role in controlling sleep and arousal. During the day, these neuropeptides stimulate other neurons to release neurotransmitters like dopamine, serotonin, and norepinephrine, promoting alertness. Reduced orexin levels can lead to excessive daytime sleepiness. People with type 1 narcolepsy have a significant reduction in orexin-producing neurons. This loss contributes to narcolepsy symptoms, including sleep paralysis, hallucinations, and cataplexy. Although weight gain isn't a direct symptom, narcolepsy patients are more likely to be overweight. Some studies suggest that orexin deficiency may be implicated in OSA. Low levels of orexin-A have been documented in OSA patients, and these levels decrease with disease severity. The orexin role in depression-When orexin levels are imbalanced, it can lead to mood disorders. Both excessive and insufficient orexin activity have been linked to depression and anxiety. Orexins influence mood through their action in the hippocampus, a brain region involved in emotion regulation. Dysregulation in orexin signaling can disrupt the balance of neurotransmitters like serotonin and dopamine, which are critical for maintaining a stable mood.

Conclusion and remarks

The interplay between OSA and depression underscores the importance of a comprehensive approach to diagnosis and treatment. By addressing both conditions simultaneously, the healthcare providers can significantly enhance patients' quality of life, encouraging using CPAP, exercise and diet. Addressing obesity through lifestyle changes, such as diet and exercise, can help manage both OSA and depression. Understanding the

symptom overlap between OSA and depression is crucial for accurate diagnosis and effective treatment. By recognizing the interconnected nature of these conditions, healthcare providers can develop comprehensive treatment plans that address the full spectrum of symptoms, ultimately improving patient outcomes and quality of life. Understanding these age-related factors can help in the early identification and management of both OSA and depression. Understanding these family factors can be crucial in the prevention and management of both depression and OSA.

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