

HOW WELL DO WE SLEEP? – REVIEW OF SLEEP QUALITY AND ITS IMPORTANCE IN MENTAL HEALTH DISORDERS

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received: 03.02.2025;

revised: 04.03.2025;

accepted: 15.07.2025

SUMMARY

Introduction: Sleep quality as a basic physiological need can be challenged in patients diagnosed with serious mental health disorders. Sleep disorders such as nightmares and insomnia can affect individuals greatly and in various ways, in some cases resulting in exacerbation of their primary mental health disorder. We took a closer look into the treatment of sleep disorders, focusing mainly on pharmacological treatment.

Methods: This review included three international databases were searched, with appropriate key words (sleep quality, sleep disorder, mental health disorder, pharmacological treatment, medicine). Literature no older than 10 years was consulted, limited to English language.

Results: Seven articles matched our search, where we got a closer look into pharmacological approaches in the treatment of sleep disorders. Results show the effects of variety of medicaments. In the treatment of insomnia olanzapine, quetiapine, zolpidem, trazodone and dimidazenil showed to be effective. Gabapentin has shown to be as effective as clonazepam in the treatment of sleep disturbances in depression. For the treatment of nightmares, prazosine and hydroxyzine showed effect in certain trials. However, this type of treatment combined with other, non-pharmacological approaches, such as cognitive behavioral therapy shows to be much more effective.

Conclusion: Effective treatment often combines pharmacological and non-pharmacological approaches, with a wide range of medications, including antipsychotics, antidepressants, benzodiazepines, and non-psychofarmacologic drugs, tailored to the specific disorder and sleep issue.

Key words: schizophrenia; post traumatic sleep disorder; depression; treatment; sleep quality.

INTRODUCTION

Representing one of the important basic physiological needs and a complex construct, sleep and sleep quality are a widely researched topic in the literature (Buysee et al. 1989, Fabbri et al. 2021, Irwin, 2015). Sleep represents a physiological, reversible state of rest characterized by reduced consciousness, limited sensory activity, and decreased voluntary muscle activity, during which the body recovers, regenerates with an aim of preparing for the upcoming everyday challenges (Buysse 2014). Taking into consideration the complexity of sleep quality, through concept analyses, sleep quality can be defined as an individual's overall satisfaction with various aspects of their sleep experience, assessed through numerous factors such as sleep efficiency, sleep latency, wake after sleep onset, and objective sleep architecture measures. It plays an essential role in maintaining health and well-being (Nelson et al. 2022). In the modern, busy world, sleep quantity shows a decrease, with an effect on its quality as well. The golden 8 hours of sleep a day seem to vary depending on the lifestyle, environment, physical and mental health status. However, sleep quality plays a more significant role in day to day life of an individual (Crivello et al. 2019, Kohyama 2021).

The well-known sleep structure, consisting of two basic phases: non-rapid eye movement sleep (NREM) and rapid eye movement (REM) sleep, is stimulated by brain's natural regulatory cycles. Naturally, throughout the night, we go through several cycles of these basic cycles which provide various benefits in regeneration of the body and mind. Disruption of this sleep pattern can affect its quality greatly, showing a negative effect on individual's daily functioning (Carley & Farabi 2016, Diagnostic and Statistical Manual of Mental Disorders 1994, Irwin 2015).

When it comes to measuring sleep quality, in practice we have subjective and objective methods (Crivello et al. 2019, Carley & Farabi 2016, Barbato 2021). The golden standard for objective evaluation of sleep quality is polysomnography (PSG), consisting of electroencephalogram (EEG), electrooculography (EOG), and electromyography (EMG).

It measures NREM stages 1 and 2, slow wave sleep (NREM stages 3 and 4) as well as rapid eye movement (REM) stage over the duration of sleep (Crivello et al. 2019, Barbato 2021, Irwin 2015).

On the other hand, subjective sleep quality measures fill in the gaps the objective measures can't reach. Despite the lack of its standard format, the gold standard for subjective sleep evaluation is sleep diary. It provides

insight into various details of one's night's sleep. Self-report questionnaires such as Pittsburgh's Sleep Quality Index (PSQI), with their pre-defined formats, represent great tools for getting information of special interest, focusing on different variables of sleep quality such as total sleep time, sleep onset latency, sleep efficiency, difficulties falling asleep, disturbances, medication use, and various others (Buysse et al. 1984, Crivello et al. 2019).

In this paper, we focus on exploring sleep quality, sleep disorders and the effects they have on mental health, as well as discuss the characteristics of pharmacological approaches in the treatment of sleep disorders among people diagnosed with serious mental health disorders, schizophrenia, depression and posttraumatic stress disorder in particular.

SLEEP DISORDERS AMONG SERIOUS MENTAL HEALTH DISORDERS

Changes in sleep patterns and sleep quality can lead to variety of potentially dangerous sleep disorders and even mental illnesses. Sometimes poor sleep quality is a consequence of other illnesses, but can also be their trigger or an initiator. More and more attention is paid to effects sleep has on mental health. Research recognizes the association of sleep disturbances not only with neurocognitive dysfunctions, attention deficits, struggles with cognitive performances but also with mental health disorders such as depression, anxiety, stress, schizophrenia and various others (Fabbri et al. 2021, Freeman et al. 2020, Mollayeva et al. 2016). In objective screening methods, sleep depth and REM variables are shown to be predictors of existing psychiatric comorbidity processes (Baglioni et al. 2016). Inclusion of various sleep quality treatments in the standard mental health disorders treatment may bring significant improvements in the overall mental health (Scott et al. 2021).

The main problems individuals diagnosed with a serious mental health disorder face are inadequate sleep during the night often resulting in insomnia, followed by impaired daytime functioning, also known as daytime sleepiness; sleep disturbances such as waking up, nightmares, snoring, sleep walking, muscle tension and various others (Fabbri et al. 2021).

Sleep is also shown to be a predictor of good socio-occupational functioning, which in individuals diagnosed with a serious mental illness may be compromised (Stafford et al. 2024) Among mental health disorders nightmares and insomnia are the most frequent sleep disorders to occur (Akkaoui et al. 2020).

1. Schizophrenia

Among people diagnosed with schizophrenia sleep disturbances are greatly present. Sleep disorders are not only prevalent in early psychosis, but also have effects on

psychotic episodes, increasing their frequency and intensity (Davies et al. 2017, Freeman et al. 2020). Polysomnographic testing showed lower total sleep time and sleep efficiency, prolonged sleep onset latency and total awake time, as well as increase in stage one NREM, meanwhile the remaining sleep stages, including REM sleep are reduced. REM sleep can vary on the duration of the disorder, where a decrease in REM sleep was recorded in patients with a diagnosis of schizophrenia of over three years (Chan et al. 2017). Rapid eye movement stage in patients diagnosed with schizophrenia is characterized with shortened REM latency and increased REM density, which means that they enter the REM stage quickly but the eye movement activity is increased, which may result in more vivid dreams (Baglioni et al. 2016, Barbato 2023, Chan et al. 2017). Increased REM density could also be a predictor of insomnia (Barbato 2023).

When it comes to sleep disorders, insomnia, nightmares, troubles staying asleep, hypersomnia and irregular sleep patterns are most often recorded (Freeman et al. 2020, Seeman 2018, Waite et al. 2020). Nightmares in people diagnosed with schizophrenia come in more vivid scenarios, leaving a bigger impact than they would on an individual with no comorbidities regarding their mental health. Their importance is significant due to warning signs they give out, upcoming psychotic episode, cognitive decline, increased delusions, as well as risk of suicide. However, in the assessment and further patient's therapy, they're rarely discussed (Akkaoui et al. 2020, Seeman 2018).

2. Depression

Individuals diagnosed with depression commonly report changes in their sleep patterns, ranging from inability to fall asleep to hypersomnia, where they escape into sleep to manage the effect of symptoms the depression carries. When it comes to polysomnographic testing, the changes in REM sleep are noticeable.

The alteration of REM sleep is present in all its variables: latency, density and duration (Baglioni et al. 2016) REM latency is shortened, meanwhile the duration of REM sleep is prolonged and REM sleep intensity is increased (Baglioni et al. 2016, Barbato 2023, Seithikurippu et al. 2020).

In the typical symptomatology of depression, insomnia is the most common sleep disorder, affecting the individual's processes of thoughts, as well as daily functioning. However, in the atypical symptomatology, hypersomnia, defined as excessive sleepiness or prolonged sleep duration, as well as increased daytime sleepiness, can be present. In this subtype of depression are symptoms like mood reactivity, increased appetite, and sensitivity to rejection, also included (Murphy & Peterson 2015, Plante et al 2017).

When it comes to depression as a segment of bipolar disorder, changes in REM correlate to changes in mood of individuals diagnosed with bipolar disorder, exhibiting

in more early awakenings and less rapid eye movements, which can be a predictor of an upcoming depressive phase. In individuals with bipolar disorder, the density of the REM phase has shown to be significantly higher (Barbato 2023).

Frequent nightmares, which in people diagnosed with depression are doubled, compared to the healthy population, especially the vivid ones, can contribute to increased suicidality, or even suicide attempts among people with depression. In comparison to bipolar depression, nightmares are more frequent in individuals with unipolar depression (Akkaoui et al. 2020).

3. Post-traumatic stress disorders

Patients with post-traumatic stress disorder (PTSD) exhibit significant sleep dysfunctions, particularly in REM sleep. Meta-analytic reviews highlight that PTSD patients experience greater REM density, more stage 1 sleep, and reduced slow wave sleep compared to healthy individuals. Increased REM density persists even in chronic PTSD cases spanning decades and is notably higher in these patients compared to those with depressive disorders, though trauma-related nightmares correlate more with REM interruptions than density (Barbato 2023). Additionally, polysomnographic studies reveal decreased total sleep time, slow wave sleep, and sleep efficiency, alongside increased wake time after sleep onset in PTSD patients. Sleep efficiency and slow

wave sleep percentage decline with greater PTSD severity, while REM sleep percentage is reduced in younger PTSD patients but not in older age groups. These findings confirm pervasive sleep abnormalities in PTSD (Barbato 2023, Zhang et al. 2019).

Nightmares are an important part of post-traumatic stress disorder, affecting up to 70% of diagnosed patients, which correlates with the severity of the disorder. Severity of the nightmares can sometimes lead to suicidal behavior as well (Akkaoui et al. 2020).

TREATMENT OF SLEEP DISORDERS

1. Pharmacological therapy

The results indicate that sleep disorders, including insomnia and nightmares, can be effectively managed through pharmacological treatments. Notably, a single class of medications is not solely responsible for achieving positive outcomes. Instead, various medication groups, used in combinations and tailored dosages, offer promising solutions for treating these conditions.

We highlighted several pharmacological approaches that align with our aims and are focused on the treatment of sleep disorders among psychiatric disorders, with various outcomes, from which the majority were quite effective (Table 1).

Table 1. Summary of pharmacological therapy for sleep disorders.

Authors	Research type	Interventions	Results
Feng et al. 2024	Meta-analysis	Olanzapine, quetiapine 50-800mg/day	effect in reduction of insomnia in sleep disorders among individuals diagnosed with psychotic disorders
Morin et al. 2023	RCT	1 st stage CBT + Zolpidem (5-10mg/d) for 6 weeks 2 nd stage = CBT + trazodone (50-150mg/d)	reduced daytime symptoms of insomnia improvement in daytime functions among healthy individuals as well as among those with a psychiatric comorbidity
Huang et al. 2024	Meta-analysis	Prazosine 1-15mg /day for 8 weeks Hydroxyzine 10-100mg /day for 8 weeks	reduced nightmare severity in individuals diagnosed with PTSD
Mowla et al. 2015	RCT	Gabapentin (100–600 mg/day) or Clonazepam (0.5–2 mg/day) / weeks along with current antidepressant therapy (sertraline, fluoxetine, citalopram)	Gabapentin has shown to be as effective as clonazepam in treatment of sleep disturbances in individuals diagnosed with depression
Raskind et al. 2018	RCT	Prazosine 2-15mg / day for 16 weeks	no significant effect on trauma-related nightmares in military veterans with a diagnose of PTSD
Kishi et al. 2024	Systematic review	Dual orexin receptor antagonists (DORAs) – suvorexant and lemborexant	No significant effect on insomnia in individuals diagnosed with psychiatric disorders
Ran et al. 2024	Systematic review	Dimdazenil 1.5 - 5 mg /day up to 2 weeks	Significant effect in reduction of insomnia (presence of psychiatric diagnoses was not specified)

Quetiapine, a medication from antipsychotic group used mainly in the treatment of psychotic disorders, showed positive effects in reduction of insomnia, along with olanzapine which contributed to good regulation of not only insomnia, but mania as well (Feng et al. 2024). These results show the universality of antipsychotic drugs, where, instead of the focus on their antipsychotic effects, their other qualities come into light. Dependable on the dose, these medicaments could potentially show an excellent effect in the treatment of sleep disorders among other psychiatric disorders as well, with calculated doses in the combination with their existing treatment, focusing on the individual needs of the patient.

Morin et al. (2023) report positive effects of a non-benzodiazepine sedative-hypnotic, zolpidem treatment combined with cognitive behavioral therapy for reducing insomnia symptoms in comparison to the control group using only behavioral therapies for insomnia. The second stage of their trial included a serotonin receptor antagonists and reuptake inhibitor medication, trazodone for non-remitters, after a 6 week therapy with zolpidem, with a controlled withdrawal schedule. The shift to trazodone contributed to increased daytime functions of individuals.

Huang et al. (2024) report reduction of nightmare severity in people with post-traumatic stress disorder while on prazosin and hydroxyzine treatment. Prazosin, a medication mainly known as an antihypertensive agent, has a significant effect in the treatment of nightmares as well, along with hydroxyzine, an antihistamine, in this case have shown to be of bigger priority in treatment of nightmares than other approaches. (Huang et al. 2024). However, in the trial including military veterans with posttraumatic stress disorders and trauma induced nightmares, prazosin as a medicine of choice hasn't shown significant effects on reducing the nightmare frequency and intensity (Raskind et al. 2018).

In comparison to clonazepam, which is a benzodiazepine medicament, with addictive side effects, gabapentin, an antiepileptic drug, has shown equal potency in regulating sleep problems in people diagnosed with depression, with lower risk of developing addiction (Mowla et al. 2015).

Dual orexin receptor antagonists (DORAs) work by blocking the both orexin receptors in the brain, which are in charge of regulating wakefulness, arousal and appetite, therefore, they have shown to be a safe and tolerable option in the treatment of sleeping problems in people diagnosed with mental disorders, even though the reviewed medications, suvorexant and lemborexant, haven't shown a very significant effect in the treatment of insomnia in particular (Kishi et al. 2024). The safety of these drugs offers a good path for the future testing, in potential combinations with other medicaments or for the purposes of the achieved treatments' maintenance.

Dimidazenil, as a benzodiazepine derivivate with a moderate GABA α receptors activation, has shown significant improvement in certain objective and subjective sleep outcomes in individuals with insomnia,

such as reduced sleep latency and increased total sleep time. These benefits stand out because there was no significant excessive daytime sleepiness or impairment of daytime functioning happening. Additionally, it has shown to be a very tolerable medication (Ran et al. 2024). By exploring the findings, with a focus on the cause of the insomnia, whether it be a underlying psychiatric diagnosis or a lifestyle obstacle, these results could be of an even bigger benefit to the future efficacy of dimidazenil as a medicament for sleep disorders' treatment.

The consulted literature emphasizes the presence of non-pharmacological approaches, mainly cognitive behavioral therapy in the treatment of sleep disorders, which is definitely an important segment of the treatment. Various methods of cognitive behavioral therapy can be applied and at the same time be very effective, especially if they're personalized, matching the person's habits, interests and wishes.

2. Non-pharmacological treatment

We can't forget the importance of non-pharmacological approaches in the treatment of sleep disorders in people diagnosed with mental health disorders. To make pharmacological treatment show its best results, another approaches are included such as cognitive behavioral therapy, exercising, or some other alternative approaches. In many examples, cognitive behavioral therapy is considered a first line treatment, often applied together with medicaments. However, it comes in different forms and shapes, created according to the individual's needs (Hertenstein et al. 2022).

2.1. Cognitive behavioral therapy

Cognitive behavioral therapy in treating sleep disorders consists of sets of steps, aimed to modify one's daily habits related to sleep. In patients with mental health disorders, treatment is based on individual needs and triggers. Basic CBT techniques consist of ensuring adequate environment, stimulus control, stabilizing circadian rhythm, getting the bedtime routine in check, relaxation and productive daytime activities. Additionally, specific cognitive techniques can be included, such as imagery rehearsal, grounding techniques and reduction of hypnotic medicaments (Waite et al. 2016). Randomized controlled studies involving cognitive behavioral therapy for sleep disorders in the population of patients diagnosed with serious mental health disorder, report positive results regarding the reduction of sleep disorders, particularly nightmares and insomnia (Sheaves et al. 2019).

Image rehearsal therapy as a component of cognitive behavioral therapy, shows great results in the treatment of nightmares. It is based on rehearsing dreams, where individuals practice reshaping the nightmares they have into less disturbing dreams with a positive ending by imagining it on several occasions during the day (Van Schagen et al. 2016).

Sheaves et al. (2019), in their randomized controlled trial of imagery-focused cognitive therapy approach, report great patient satisfaction and reduction of nightmare severity, comorbid insomnia and persecutory delusions in their follow up assessments.

There is a noticeable positive response to cognitive behavioral therapy treatment for insomnia and nightmares in patients with psychosis, depressive disorders and post-traumatic stress disorders (Huang et al. 2024, Seeman 2018). Cognitive behavioral therapy is characterized with multiple different combinations of approaches, which can be adjusted to the individual's needs. We once again emphasize that the important segment of cognitive behavioral therapy is the collaboration with the patient, valuing and respecting their needs, habits, as well as wishes. Optimizing this kind of approach might not always be easy, but once done, can show great results.

2.2. Controlled sleep deprivation and sleep restriction

Sleep restriction, or restricting the time in bed, is a component of cognitive behavioral therapy for insomnia, which is based on restricting time spent in bed (Falloon et al. 2015, Steinmetz, et al. 2023). Short term effects on insomnia were reported in various samples. However, it shows a promising treatment method for long term effects in treatment of insomnia (Falloon et al. 2015, Kalmbach et al. 2019, Maurer et al. 2021).

Sleep deprivation, on the other hand, focuses on intentional sleep restriction, where an individual remain awake through the night with an aim to reset the circadian rhythm. It can be a complete or partial, depending on the severity of the sleep disturbance. As an addition to standard treatment, its effect is shown in short term alleviation of depressive symptoms in individuals diagnosed with depression or bipolar depression (He et al. 2023, Ioannou et al. 2021, Ramirez-Mahaluf et al. 2020, Xu et al. 2024). In some cases, improved effect of pharmacological therapy in combination with sleep deprivation, was reported (Ramirez-Mahaluf et al. 2020). With little to no side effects, this method is safe to use for depressive disorders, but not recommended for psychosis, due to risk of triggering a psychotic episode (Meyhöfer et al. 2017). As healthcare professionals, instead of primarily focusing on the mental or sleep disorder itself, our duty is to observe the person as a whole with all of their attributes, needs, and wishes, in order to provide the optimal, person centered, holistic care.

2.3. Other approaches

Acupuncture, a complementary medicine based approach, as an addition to the regular treatment of sleep disorders, has shown moderate positive results in treatment of insomnia, with minimal to no side effects to the patients (Bergdahl et al. 2016, Chung et al. 2018, Lee et al. 2020). Lucid dreaming therapy has shown some potential in the reduction of nightmare intensity (Ouchene et al. 2023). Regular exercise, low-impact cardio and resistance in particular, showed a significant improvement in sleep

quality as well as quality of life in people diagnosed with schizophrenia (Tous-Espelosin et al. 2024, Xie et al. 2021). In addition to psychotherapeutic and pharmacological treatment, yoga as a form low impact exercise has shown to be helpful in insomnia management, as well as in improvement of everyday quality of life in people with serious mental health disorders (Bhatia et al. 2022, Broderick et al. 2017, Verma et al. 2022, Yin et al. 2024). Offering a variety of options to the individuals with sleep disorders helps them contribute to their own healing journey, improving their motivation and day to day life.

CONCLUSION

Sleep disorders in people diagnosed with serious mental health disorders are inevitable, followed by symptoms which can contribute to the development or exacerbation of the disorders themselves. Most common ones are insomnia and nightmares, which impact the daytime functioning greatly. Treatment of sleep disorders in the population of people with mental health disorders focuses mainly on non-pharmacological and pharmacological approaches, which in combination bring the optimal results. The pharmacological approaches vary depending on the mental health disorder itself and the existing sleep disorder. It's shown that a good variety of effective medicines exist, from antipsychotic and antidepressant drugs, to benzodiazepines, non-benzodiazepines, as well as other, non-psycho pharmacologic, drug groups. The combination of adequate doses of medicaments, in combination of approaches for improving life quality can benefit the affected population greatly.

Limitations and suggestions for future research

In this review, the focus was mainly on schizophrenia, depression and posttraumatic stress disorder, whereas sleeping problems persist in other mental health disorders as well. Expansion of sources is a goal for the future, more extensive literature reviews, meta-analyses even.

Acknowledgements: None.

Conflict of interests: None.

Contributors:

Marijana Gajić: conceptualization, methodology, manuscript writing,

Nuša Kirbiš: conceptualization, data collection.

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