

# Sleep disturbance: a potential target to improve symptoms and quality of life in those living with psychosis

*Sleep that knits up the ravelled sleeve of care, the death of each day's life, sore labour's bath, balm of hurt minds, great nature's second course, chief nourisher in life's feast*

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Sleep has been shown to impact on both physical and mental health, and sleep problems present a considerable burden for individuals and society. There appears to be a complex bidirectional relationship between sleep disturbance and psychiatric symptoms, each potentially influencing the other. In particular, sleep disorders have been associated with more severe symptoms and are predictive of relapse in those with psychotic disorders. This article discusses the relationship between psychosis and insomnia, sleep apnoea, nightmares, circadian rhythm abnormalities and the impact of medications on these relationships. We also discuss the clinical implications of the relationship between sleep disturbance and psychotic disorders along with potential targets for intervention.

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## Introduction

Sleep plays an important role in memory consolidation, emotional regulation, immune function and metabolic homeostasis (Baglioni *et al.* 2010; Irwin *et al.* 2010; Payne & Kensinger, 2010; Xie *et al.* 2013). Sleep disturbance may represent an aetiological factor and symptom of many psychiatric disorders (Baglioni *et al.* 2011; Anderson & Bradley, 2013). Insomnia, the most researched sleep disorder is common, severe and treatable in patients with serious mental illness (Taylor & Pruiksma, 2014) with the prevalence rates of 16–44% (Lieberman *et al.* 2005; Xiang *et al.* 2009; Palmese *et al.* 2011; Subramaniam *et al.* 2018) compared to 3–6% in the general population (Calem *et al.* 2012). Many patients report sleep disturbance as a warning sign of relapse in psychotic symptoms (Harvey, 2008; Freeman *et al.* 2009). Sleep disorders in early psychosis have been associated with increased psychotic experiences, anxiety, depression, fatigue and lower quality of life (Reeve *et al.* 2019).

## Sleep disturbance in psychosis

Sleep disturbance is found in 30–80% of patients with psychosis (Tandon *et al.* 1992; Keshavan & Tandon, 1993; Cohrs, 2008). It is a core feature of bipolar affective disorder (BPAD) (World Health Organization, 1992) and commonly occurs during episodes of mania and depression. Sleep disturbance may continue during inter-episode euthymic periods. Such baseline sleep disturbance is associated with a poorer prognosis (Kaplan *et al.* 2011; Sylvia *et al.* 2018). Insomnia may be a causal factor in the occurrence of psychotic experiences and is inversely correlated with quality of life (Xiang *et al.* 2009; Freeman *et al.* 2010; Reeve *et al.* 2015). Sleep difficulties, particularly insomnia, are associated with more severe psychotic symptoms in patients with schizophrenia and are predictive of relapse and transition from 'at risk mental state' to first-episode psychosis (Poulin *et al.* 2003; Reeve *et al.* 2015). Insomnia may frequently co-occur with nightmares, circadian dysfunction, parasomnias, etc. in individuals with schizophrenia (Chiu *et al.* 2016). Studies have shown an association between insomnia and suicidal ideation, suicidal attempts, completed suicide and psychopathology in patients with schizophrenia (Pompili *et al.* 2009; Li *et al.* 2016; Miller *et al.* 2019).

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Approximately 10–55% of people with schizophrenia report frequent nightmares (Mume, 2009; Michels *et al.* 2014; Sheaves *et al.* 2015) compared to the general population rate of approximately 2–6% (Li *et al.* 2010; Sandman *et al.* 2013). The continuity hypothesis of dreaming suggests that waking life experiences are reflected in dreams under particular conditions (Schredl, 2003). A study on acutely psychotic inpatients found that there was continuity between dream and waking mentation for specific single recurring delusional themes (grandiosity and religion), suggesting an association between specific delusional contents and dreams (D'Agostino *et al.* 2013). Nightmares have been associated with increased suicidal ideation and behaviour (Pigeon *et al.* 2012; Nadorff *et al.* 2016; Titus *et al.* 2018). Comorbid nightmares and insomnia were associated with an increased suicide risk above either disorder individually in people with schizophrenia (Li *et al.* 2016).

Rates of obstructive sleep apnoea (OSA) are elevated in individuals with schizophrenia and around 15% demonstrate clinically significant symptoms (Anderson *et al.* 2002). OSA may be mediated by weight gain, neuroleptic medication and lifestyle factors. Marked circadian rhythm abnormalities have been shown in schizophrenia (Wulff *et al.* 2012) and BPAD (Millar *et al.* 2004; Jones *et al.* 2005). This may be due to dopamine dysregulation (Yates, 2016). Circadian rhythm disturbance has been associated with elevated rates of cancer, diabetes, cardiovascular disease and obesity (Touitou *et al.* 2017). It can increase risk of accidents, errors in the workplace (Folkard *et al.* 2005; Van Dongen *et al.* 2016) and impact on personal life and general well-being (James *et al.* 2017). Given the widespread potential impact, treatment of circadian rhythm disturbance is an important target for intervention (Lewis *et al.* 2016; Yates, 2016).

### Neurophysiological abnormalities

A number of sleep parameters, for example, amount of slow-wave sleep (SWS) and Rapid Eye Movement (REM) latency, are correlated with clinical variables in schizophrenia, including severity of illness, positive symptoms, negative symptoms, neurocognitive impairment and brain structure (Poulin *et al.* 2003; Chouinard *et al.* 2004). Memory consolidation has been shown to be impaired in schizophrenia and positively correlated with sleep efficiency and the amount of SWS (Goder *et al.* 2004). Decreased slow-wave density has been reported in acutely psychotic patients (Ganguli *et al.* 1987; Keshavan *et al.* 1998) and first-episode psychosis is inversely correlated with positive symptom severity (Kaskie *et al.* 2019a). This is in contrast to more stable patients with schizophrenia

(Goder *et al.* 2015). Deficits in sleep spindle activity have been consistently shown in first-episode psychosis and schizophrenia; however, slow-wave deficits have been less consistently found (Castelnovo *et al.* 2018; Kaskie *et al.* 2019b). Unaffected first degree relatives of those with schizophrenia have been shown to have non-REM sleep abnormalities including reduced spindle activity and decreased slow-wave amplitude (D'Agostino *et al.* 2018). The authors propose that disrupted cortical synchronisation (slow-wave activity) may increase risk and that thalamic dysfunction (reduced spindle activity) may also be necessary to develop schizophrenia. Sleep abnormalities present in psychosis may interfere with memory consolidation and influence cognitive function, mood and psychotic symptoms. However, further research is necessary to determine the direction of associations.

### Medications

Sedatives and antipsychotics are commonly prescribed for sleep problems. However, sedative medications have limited effectiveness in chronic insomnia and have been associated with nightmares (Pagel & Helfter, 2003), risks of drug interaction, dependence and adverse side effects (Holbrook *et al.* 2000; Cates *et al.* 2009; Takaesu *et al.* 2014). Both first and second generation antipsychotics (except risperidone) have been associated with prolonged total sleep time and increased sleep efficiency in schizophrenia (Cohrs, 2008; Monti *et al.* 2017).

Furthermore, second generation antipsychotics reduce sleep latency and may offer some relief from chronic insomnia in those with schizophrenia (Monti *et al.* 2017). However, the confounding effect of antipsychotics in individual sleep disorders, particularly movement disorders and sleep-related breathing disorders, and the possibility of daytime sedation are major problems (Cohrs, 2008). This picture is complicated by antidepressants' interaction with sleep as they are often prescribed alongside antipsychotics (Wilson & Argyropoulos, 2005).

### Future interventions

Treating sleep is an important therapeutic target in psychosis. Guidelines are in place stating that clinically significant sleep disorders should be considered as comorbid diagnosis and receive independent clinical attention regardless of other conditions (APA, 2013; AASS, 2014). Cognitive behavioural therapy for insomnia (CBT-I) has an established evidence base (Trauer *et al.* 2015; Riemann *et al.* 2017), has been used to treat insomnia in psychosis and may reduce psychotic symptoms (Freeman *et al.* 2015; Chiu *et al.* 2018;

Hwang *et al.* 2019). Furthermore, treatment of nightmares using proven techniques such as image rehearsal therapy or CBT for nightmares may alleviate psychotic symptoms along with nightmares themselves (Seeman, 2018; Sheaves *et al.* 2019).

Despite the high prevalence of sleep disorders in psychosis and improving sleep being among patients' highest priorities for treatment (Waite *et al.* 2015), sleep disorders are rarely addressed directly. Manifestations of daytime symptoms stemming from insomnia can be important illness indications (Cheung *et al.* 2014). A recent study showed that while over half of those with sleep disorders had discussed this with a clinician, almost 60% received no treatment (Reeve *et al.* 2019). Treatment of sleep disorders is a priority for patients with psychosis (Faulkner & Bee, 2017). However, formal sleep assessments are rarely used and evidence-based treatments such as CBT-I are infrequently offered (Cheung *et al.* 2014; Rehman *et al.* 2017). Qualitative studies show that patients show a preference for cognitive and behavioural therapies over standard pharmacological or melatonin-based therapies for long-term sleep problems (Waters *et al.* 2015; Chiu *et al.* 2016; Faulkner & Bee, 2017). An important consideration is that people with schizophrenia are likely to require support with motivation and further psychological interventions to address unhelpful cognitions about sleep (Chiu *et al.* 2016). A recent adaptation of CBT-I in psychosis incorporates 12 main factors which disrupt sleep in those with schizophrenia and patients' concerns regarding treatment (Waite *et al.* 2016). This may act as a building block to future therapies.

Light therapies represent a potential mechanism to improve circadian rhythm sleep disorders (Faulkner *et al.* 2019). However, further research is needed in those with psychosis. The majority of females with schizophrenia who have OSA are never diagnosed clinically, despite the potential benefits of continuous positive airway pressure on cardiometabolic parameters and cognitive impairment (Seeman, 2014). Increased awareness of symptoms of hypersomnia such as excessive daytime sleepiness and extended nocturnal sleep period along with lack of energy, depression and insomnia in this population may help improve clinical suspicion (Hawley, 2006).

Evidence to date can only confirm that the relationship between sleep disorders and psychosis is at an associative level (Reeve *et al.* 2015; Davies *et al.* 2017). Nonetheless, sleep disturbance in psychosis should be a target for intervention, since it is a source of distress and impaired functioning for which effective treatments exist (Waite *et al.* 2016; Freeman *et al.* 2017). However, as different sleep disorders require different and specific interventions, establishing the prevalence and types of sleep disorders and the acceptability of

potential interventions should now be regarded as a crucial avenue of investigation in psychosis research.

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### Conflict of Interest

The authors have no conflicts of interest to declare.

### Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that ethical approval for publication of this paper was not required by their local REC.

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