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CLINICAL REVIEW

A systematic review of the nature and correlates of sleep disturbance in early psychosis

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SUMMARY

Sleep disturbances are common in people with a diagnosis of schizophrenia and have been associated with increased symptom severity, neurocognitive deficits and reduced quality of life. Despite a significant body of literature in this field, there has been limited investigation of sleep disturbance in the early course of the illness. This systematic review aims to synthesise and evaluate the available data exploring sleep in early psychosis, with two key research questions: 1) *What is the nature of sleep disturbance in early psychosis?* and 2) *What are the correlates of sleep disturbance in early psychosis?* From an initial search, 16,675 papers were identified, of which 21 met inclusion/exclusion criteria. The preliminary evidence suggests that self-reported sleep disturbances are prevalent in early psychosis and may be associated with symptom severity, as well as elevated rates of both help-seeking and suicidality. Abnormalities in sleep architecture and sleep spindles are also commonly observed and may correlate with symptom severity and neurocognitive deficits. However, due to significant methodological limitations and considerable heterogeneity across studies, evidence to support the reliability of these associations is limited. We outline a research agenda, emphasising the prospective use of gold-standard sleep measurement to investigate the prevalence and nature of sleep disturbances in early psychosis, as well as how these may be related to the onset and persistence of psychotic symptoms.

Introduction

Schizophrenia and early psychosis

Schizophrenia affects approximately 1% of the general population and is associated with a total economic cost of around £12 billion per year in England alone [1]. It is characterised by persistent, distressing and disabling symptoms, associated with reduced quality of life and functioning, with relapse and hospitalisation being common [2]. According to the diagnostic and statistical manual of mental disorders, 5th edition (DSM-5) criteria, the core symptoms of schizophrenia include 'positive' symptoms (such as hallucinations, delusions and disorganised speech) and 'negative' symptoms (such as emotional withdrawal, blunted affect and anhedonia), combined with a marked reduction in functioning, present over a duration of six months or more [3]. However, given the heterogeneity and individual variability displayed in the presentation of schizophrenia, the validity of this diagnosis has been debated [4,5].

There is no clear consensus regarding the aetiology of schizophrenia, however contributors seem to include genetic, environmental and neurodevelopmental factors [6–8]. Recent work has suggested that sleep disturbances may also play a role in the onset of psychosis and exacerbation of psychotic symptoms [9–12], although the nature of this relationship remains unclear.

The first episode of psychosis is commonly experienced around age 16–35 [13] and up to 80% of these individuals will experience a

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Abbreviations

ARMS	at risk mental state
APS	attenuated psychotic symptoms
BLIPS	brief limited intermittent psychotic symptoms
BPRS	brief psychiatric rating scale
CAARMS	comprehensive assessment of at risk mental states
CBT-I	cognitive behavioural therapy for insomnia
DSM-5	diagnostic and statistical manual of mental disorders, 5th edition
EEG	electroencephalography
ESM	experience sampling method
ESS	Epworth sleepiness scale
FEP	first episode psychosis
GAF	general assessment of functioning
HR	hazard ratio
IQ	intelligence quotient
LLE	largest Lyapunov exponent
MAPP	multidimensional assessment of
MEQ	morningness-eveningness questionnaire
MRI	magnetic resonance imaging
NREM	non rapid eye movement
OSA	obstructive sleep apnoea
PLMD	period limb movement disorder
PSG	polysomnography
PSQI	Pittsburgh sleep quality index
RCT	randomised controlled trial
REM	rapid eye movement
REMOL	REM onset latency
RT	reaction time
SAPS/SANS	scale for the assessment of positive symptoms/ scale for the assessment of negative symptoms
SE	sleep efficiency
SIPS	structured interview for prodromal symptoms
SOL	sleep onset latency
SWS	slow wave sleep
TST	total sleep time
UHR	ultra high risk
WASO	wake-time after sleep onset
WCST	Wisconsin card sorting task
WRAT-R	the wide range achievement test-revised

recurrent episode within five years [14]. The first episode of psychosis is usually preceded by a prodromal period, typically characterised by features including reduced attention and motivation, feelings of depression, anxiety, social withdrawal, suspiciousness and disturbed sleep [15,16]. Those in this prodromal period are often referred to as 'ultra high risk' (UHR) or 'at risk mental state' (ARMS), based on criteria originally developed by Yung et al. [15]. These criteria have been validated in several countries and are recognised as the gold-standard for systematically screening for psychosis risk. Individuals who present as 'at risk' of developing psychosis will typically experience one or more of the following symptoms: attenuated psychotic symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS) and/or genetic risk combined with a significant reduction in functioning [17]. Of those meeting UHR/ARMS criteria, 20–30% will go on to experience frank psychosis over a 10 y period, compared to 1% of the general population [18,19]. In order to reduce the number of people who develop psychosis, and to decrease the likelihood of future relapse, research has become increasingly centred on early intervention; with a focus on developing effective treatments for the early stage of the illness, as well as identifying the key risk factors for psychosis onset and relapse [10,20,21].

Sleep and schizophrenia

Sleep disturbances have been observed in schizophrenia for almost 100 y [22]. However, they have only recently been recognised as a potential contributor to the onset and maintenance of the disorder and as a possible target for intervention [23,24]. Insomnia is commonly reported in schizophrenia, although obstructive sleep apnoea (OSA) and periodic limb movement disorder (PLMD) are other frequent complaints. Circadian patterning of sleep may also be disrupted, ranging from phase delay to complete day–night reversal [25,26]. In addition to self-reported sleep disturbances, polysomnography (PSG) studies reveal changes in sleep continuity in schizophrenia, with reductions in total sleep time (TST) and sleep efficiency (SE) being consistently reported [27,28]. On the other hand, abnormalities in sleep architecture are more variable, with a range of alterations to slow wave sleep (SWS) and rapid eye movement (REM) sleep parameters being observed, but with little consensus across studies [27,29–31].

Antipsychotic medications have been repeatedly shown to influence sleep architecture and continuity [27,32]. Both first and second generation antipsychotics can improve self-reported sleep in some cases [27], however sleep–wake cycle disruption has also been attributed to the daytime sedative effects of antipsychotic medication [33] and both OSA and PLMD have been associated with the side-effects of these medications [27,34–36]. Such effects are likely to become more pronounced with long-term administration, highlighting the potential importance of studying sleep in the early stages of schizophrenia.

Both self-reported and objectively measured sleep disturbances have been linked to reduced quality of life, cognitive deficits, poorer functioning, and both positive and negative psychotic symptoms in those with a schizophrenia diagnosis [27,37–40]; however there are relatively few experimental data to indicate a causal effect for sleep on symptomatology.

Despite the substantial literature investigating sleep disturbances in those with a long-term diagnosis of schizophrenia, sleep has received comparatively little attention in the early course of the disorder. Research within this population may be essential to enhance understanding of the aetiology of sleep disturbance in schizophrenia, especially when undertaken with individuals who are naïve, or have had limited exposure, to antipsychotic medication. Such data would permit a greater understanding of the prevalence and impact of sleep difficulties across the course of schizophrenia and whether disturbed sleep may be a factor in the maintenance of psychotic symptoms, or in relapse. Two recent reviews have presented models for the role of sleep disturbance in psychosis onset [9,11]. However these articles have not been rigorously systematic in nature and have included data from genetic risk samples and studies of longer-term schizophrenia in order to support their conclusions.

A comprehensive review of sleep disturbances in the early stages of schizophrenia is needed to synthesise available evidence and to guide future research and clinical agendas. This review focused on data derived from samples who had recently experienced the initial onset of psychosis (or 'first episode' of psychosis), and later received a schizophrenia diagnosis, or individuals with a