

Sleep Patterns in Patients with Schizophrenia: A Review

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Abstract

Introduction: Schizophrenia is a very debilitating chronic mental disorder which is characterized by positive symptoms, such as delusions and hallucinations, along with negative symptoms, established as social withdrawal and blunted affect

Methods: literature review using the pubmed database.

Results: The majority of studies showed the effect of schizophrenia on disturbing the circadian rhythm and also the sleep spindles, thus affecting the cognition of the patients.

Conclusion: Sleep disturbances in schizophrenia may be partially associated with the increased activity of the dopaminergic system in the brain, which leads to the possible role of using melatonin as a pharmacological treatment as it has been found to reduce to the dopamine activation in the brain.

Keywords: Sleep, Schizophrenia, Circadian Rhythm, Sleeps Spindles.

Introduction:

Schizophrenia is a very debilitating chronic mental disorder which is characterized by positive symptoms, such as delusions and hallucinations, along with negative symptoms, established as social withdrawal and blunted affect. Although insomnia may be a common feature in patients with schizophrenia, it's rarely addressed as the main complaint. Many sleep studies in patients with schizophrenia have been inspired by the similarities between dream and hallucinations that were observed by clinical investigators. The first to ever look at sleep in patients with schizophrenia was a German psychiatrist "Emil Kraepelin" who studied dreams and "schizophasia", known as "word-salad" nowadays, in patients with schizophrenia.¹ Difficulties in initiating or maintaining sleep are commonly found in the patients, affecting 30-80% of them, depending on the degree of the psychotic symptomatology.² There has been a spat of reports in the past few years discussing the link between schizophrenia and sleep macroarchitectural abnormalities, including prolonged sleep onset, decreased total sleep time and short REM latency. Negative symptoms have been shown to decrease the delta wave counts in patients with schizophrenia. In

addition, some studies suggested that the circadian rhythm is also disrupted, either due to the clinical outcomes of the disease or the medications taken to treat the disease itself.³

Two aspects of sleep disturbances that have been focused at, with a proven effect on cognition, were reduced sleep spindles in the electroencephalogram, and disruption of the circadian rhythm which will be discussed in details below.

Circadian rhythm³

There are many medical issues with relation to sleep pattern in schizophrenia, but the most clinically relevant and distressing problem is going to sleep while everyone else is awake. This is known as the circadian rhythm, which is more of a clock that regulates the sleep cycle in the body, and once this clock's battery burns out, the brain loses the ability to synchronize sleep with the environment. This mis-synchronization may be either attributed to the sedative effect of medications or the negative symptoms of the disease. The main influence that regulates this clock, which in turn regulates the sleep-wake cycle, is light. Patients with psychosis, including schizophrenia, may get very little light during the day as they tend to be socially withdrawn

and might keep their curtains closed since they perceive the sun light as a threat. This by itself may play a role in disrupting the sleep cycle in the brain and affect the signals that regulate the circadian rhythm.

Many studies aimed to investigate the sleep-wake cycle but failed due to the day-to day fluctuation of this event and the need for a long follow up trial to study the characteristic of such cycle. Two recent published papers in the British Journal of Psychiatry studied the sleep-wake cycle over 6 weeks, using actigraphy, which is a non-invasive method to measure the rest-activity cycles in patients with schizophrenia. In this study, there were 2 groups, the cases, who are the patients with schizophrenia, and the controls, who are healthy individuals. Both groups were asked to wear a wrist device, which measures the activity over days or weeks. Only little movement is registered during sleep, and more movement is recorded during the waking hours. The study showed that the cases had longer sleep hours than the controls during daytime, and 50% of them showed misalignment of sleep with the environmental night-time. The circadian non-synchronization was not related to the clinical state or dose of antipsychotics.

Similar findings were established in another study that looked at the frontal lobe function in the cases and controls, in which the participants who had a normal circadian rhythm performed better. This brings us to the possibility of the role of disrupted sleep in the impaired cognition of patients with schizophrenia.

These two papers, with their convincing objective evidence of abnormal circadian rhythm, and the additional finding of cognitive function being lower in people with more abnormal rhythms, may be enough to justify the use of targeted systematic chronotherapeutic treatments to aid rehabilitation following an acute episode of the illness.

Sleep architecture (sleep spindles) ³

Sleep architecture, sleep spindles and the electroencephalogram, have been left aside when

conducting research and haven't been studied thoroughly in schizophrenia like they have in depression. The main issue that lies here is that many of the antipsychotic medications used in the treatment of schizophrenia, often affect the neurophysiology of the brain, and in turn alters the sleep features. On the other hand, it is very difficult to conduct such studies in patients who aren't using any medications due to the distressing positive symptoms.

Sleep spindles were one of the first patterns that were identified in the human sleep, and can be easily recorded from the scalp over the whole night in light sleep, and decreased significantly in deep sleep and rapid eye movement sleep. Although the electroencephalogram of these spindles have been established since a long time, the link between them and learning and memory has only been established recently, mainly in Germany.

It has been established that the type and amount of these spindle is related to learning and the amount of learning is related to sleep, which in simple words may be transformed as the more sleep, the more learning and the more spindles appear on the EEG. There have been 3 published studies linking sleep spindles and cognition in schizophrenia in the past 3 years, which showed a decrease in the amplitude and duration of sleep spindles in 49 participants with schizophrenia on antipsychotic medications in comparison to 44 matched controls, and also 2 non-schizophrenia patients receiving antipsychotic medications. This showed fascinating results, in which a change in sleep parameters including sleep spindles and slow wave was documented with taking anti-psychotic medications even in normal participants. However the reduction in sleep spindles were only found in patients with schizophrenia and thus couldn't be explained by the use of antipsychotics.

Another study done by Keshavan et al showed that a group of 27 untreated patients, who were newly diagnosed, had decreased spindles which was associated with a lower performance on frontal cognitive tasks. It was previously reported that patients with schizophrenia, when compared to

controls, did not show the normal improvements in a motor task (a finger-tapping sequence) after a night's sleep. This showed that the lower the spindles number and density, the smaller the improvements that were found in the task. These studies revealed a dependable neurobiological marker in schizophrenia that showed an interrupted thalamocortical activity, which could be used as a treatment target in the future.

Melatonin.....a possible therapeutic agent in Schizophrenia?³

Several studies have shown the beneficial effect of melatonin on the initiation and maintenance of sleep. It has been recommended by the British Association of Psychopharmacology as the evidence based treatment for insomnia, parasomnia and circadian rhythm sleep disorders.

Interesting results have been concluded from several studies which showed the effect of melatonin on alternating the dopamine receptor activation. A randomized double blinded controlled trial measuring the urinary melatonin output in patients with chronic schizophrenia, and assessing the effect of melatonin on their sleep quality showed that giving 2mg melatonin increased the efficiency of sleep and decrease the cognitive impairment. This hides interesting future era for melatonin agonist research and their potential use in schizophrenia.

Antipsychotic drugs and their effect on sleep architecture and circadian rhythm?⁴

Antipsychotic medications have a role on the patients sleep patterns. First and second generation antipsychotics, with the exception of risperidone, are involved with an increase in total sleep time. The increase in slow waves varies among those 2 groups, with a documented increase upon the use of olanzapine and a decrease when using clozapine. Patients treated with clozapine had significantly high rest-activity cycles, whereas patients on classical antipsychotics such as haloperidol or flupentixol had minor to major circadian rhythm abnormalities.

Conclusion:

In conclusion, initiation and maintenance of sleep is a major issue in patients with schizophrenia regardless of their medication or the phase of disease they're at. The majority of studies showed the effect of schizophrenia on disturbing the circadian rhythm and also the sleep spindles, thus affecting the cognition of the patients. Sleep disturbances in schizophrenia may be partially associated with the increased activity of the dopaminergic system in the brain, which leads to the possible role of using melatonin as a pharmacological treatment as it has been found to reduce to the dopamine activation in the brain.⁵ It may be also possible that cognitive improvement in people with schizophrenia depends on improving sleep parameters.

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