Poor sleep behaviors may increase the risk of schizophrenia: results from a study of population in southern China

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Research Article

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Abstract

Objective: There is a strong correlation between sleep disorders and schizophrenia. However, current research has mainly focused on the treatment of sleep disorders in schizophrenic patients. Our study aims to provide a comprehensive analysis of the impact of sleep behaviors on schizophrenia from a preventive perspective and to explore optimal sleep patterns.

Methods: Based on a hospital case-control study, Logistic regression analysis, interaction analysis, Restricted cubic spline and subject work characteristic curves were used to study the relationship between sleep behaviors and schizophrenia. Sleep scores (including unhealthy sleep factors: sleep deprivation at night, insomnia, snoring, nighttime sleep patterns and excessive daytime sleepiness) were constructed and assessed.

Results: After adjusting for confounders, we found that sleep duration was less than 6 hours at night (OR=2.45, 95%CI: 1.67-3.58), sleep quality was poor (OR=3.26, 95%CI: 1.87-5.69), and irregular getting up (OR=4.07, 95%CI: 2.67-6.19) and occasional napping (OR=2.06, 95%CI: 1.12-3.81) were risk factors for schizophrenia. The length and quality of sleep at night, the length of sleep at night and the pattern of napping are also risk factors for developing schizophrenia. Finally, the optimal sleep pattern is the morning sleep pattern, with six to nine hours of sleep a night, good sleep quality, no daytime sleepiness, and no snoring.

Conclusions: Poor sleep behaviors is associated with the development of schizophrenia. Through a comprehensive assessment of poor sleep behaviors, we can obtain optimal sleep patterns. This study highlights the importance of sleep behaviors and provides a new perspective on the prevention and treatment of schizophrenia.

1. Introduction

Schizophrenia (Sc) is a serious mental illness characterized by slow progression, recurrent episodes, and high risk. In the Global Burden of Disease report, schizophrenia has emerged as a serious hazard, accounting for 1.7% of disability-related loss of life expectancy per year. In China, which has the highest burden of disease from schizophrenia in the world, the burden of disease can reach 0.39% – 0.44%.[1] The prevalence of schizophrenia had a significant increase compared to 1990. At present, the prevalence rate has reached 5.44 per 1,000 in China, which is higher than the world average prevalence rate and requires attention[2]. Furthermore, outcomes for patients with schizophrenia remain suboptimal, with only 13.5% achieving clinical and social recovery and a significantly lower life expectancy than the general population[1].

Schizophrenic patients have a higher incidence of sleep disorders than ordinary patients. The incidence of sleep disorders in schizophrenic patients has reached about 65%, which increased with the severity of psychosis. Studies have shown that 30–80% of schizophrenia patients will experience sleep
disturbances, which is one of the most common symptoms of patients\textsuperscript{3}. Previous studies have found that sleep disorders not only seriously affect patients' quality of life\textsuperscript{4}, but also exacerbate their schizophrenia symptoms and affect the regression of their illness\textsuperscript{5}. People with schizophrenia who have sleep disturbances have worse quality of life and recovery\textsuperscript{6}.

Although there is ample evidence of sleep dysfunction in people with schizophrenia, little is known about the extent to which psychotic episodes are preceded by sleep problems, or how sleep disturbances relate to symptoms in at-risk populations or to normal populations. Specifically, it is unclear whether sleep dysfunction precedes psychotic episodes or whether it represents the result of prolonged exposure to schizophrenia and its treatment (e.g., substance use or neurotoxicity)\textsuperscript{7}. If sleep problems precede a schizophrenic episode, it may represent a potential target for early identification, prevention and intervention for patients at risk of psychosis.

In a case-control polysomnography study, it was found that patients with schizophrenia had significantly shorter total sleep duration, longer sleep onset latency, increased wake time after sleep onset, reduced sleep efficiency, and reduced duration and latency of stage 4 sleep, slow wave sleep, and rapid eye movement sleep compared to healthy controls.\textsuperscript{8} Disturbed sleep is increasingly investigated as one of the most promising modifiable risk markers for psychotic disorders.\textsuperscript{7} It is a widely reported symptom\textsuperscript{9} that already tends to manifest in individuals at clinical high risk (CHR).\textsuperscript{10} Using polysomnography, Keshavan and colleagues\textsuperscript{11} observed a decrease in NREM sleep, REM percentage and REM counts/min and a trend towards disrupted continuity in CHR youth compared to healthy controls. In a prospective study of individuals at high risk of clinical psychosis, it was shown that sleep disturbance was strongly associated with elevated CHR symptoms over time and, importantly, that sleep was a significant predictor of CHR symptoms, but not vice versa, although the two-way effect sizes were similar.\textsuperscript{12} Studies have also found that CHR individuals reported greater sleep disturbance than healthy controls and that the severity of sleep disturbance was positively associated with concurrent severity of attenuated psychotic symptoms.\textsuperscript{13} Based on these findings, it is clear that sleep dysfunction may be a determinant in predicting the development of psychiatric disorders in high-risk populations.

Although there is substantial evidence of a causal association between schizophrenia and sleep disorders, the direction of causation has not been conclusively established. Moreover, most of the current research\textsuperscript{14–16} on sleep disorders in schizophrenia has focused on treatment, and there is no conclusive evidence as to whether sleep disorders contribute to the development of schizophrenia. This study will provide a more comprehensive analysis of the relationship between poor sleep behaviors and schizophrenia, including nighttime sleep duration, sleep quality, naps, sleep patterns and sleep types, and analyze optimal sleep patterns to provide some theoretical support for reducing the occurrence of schizophrenia and lowering the burden of the disease, with public health and practical implications for preventing schizophrenia and improving people's health.

2. Method
2.1 Participants

A hospital-based case-control study was used. According to the inclusion and exclusion criteria, the research subjects were selected from the Fourth Hospital of Fuzhou as cases and the Union Hospital affiliated to Fujian Medical University as controls, and a questionnaire survey was conducted from May 2021 to March 2023.

The case group consisted of 507 patients with schizophrenia from the Fourth Hospital of Fuzhou (Fuzhou Mental Health Center), all of whom met the following inclusion criteria: those who met the ICD-10 diagnostic criteria for schizophrenia and signed the informed consent form. The following patients were excluded: (i) patients with other psychiatric disorders; (ii) patients with neurological disorders such as traumatic brain injury, AD, Parkinson's and mental retardation; (iii) patients with psychoactive substance abuse; (iv) patients who had undergone convulsive-free electroconvulsive therapy (MECT) before enrollment (within 90 days); (v) patients and their families (guardians) did not agree to sign the informed consent form.

In the control group, 552 patients from the Union Hospital of Fujian Medical University were selected from the same period of hospitalization, and all patients with psychiatric disorders, severe organic brain lesions, severe heart failure, malignant tumors, endocrine system diseases, recent infections, and other major diseases and those who did not agree to participate in this study were excluded.

All participants lived in Fujian for ages and signed an informed consent form. This research has been approved by the Ethics Committee of Fujian Provincial Hospital (No. K2021-04-078).

2.2 Sleep behaviors

The sleep behavior survey included the Pittsburgh Sleep Quality Index Inventory (PSQI) (this scale was developed by Buysse, Reynolds, Monk,Berman and Kupfer (1989) and consists of 7 components, each with a score ranging from 0 (no difficulty) to 3 (severe difficulty). These 7 components are: "sleep quality", "sleep latency", "sleep duration", "sleep efficiency", "sleep disturbance", "sleep medication use", and "daytime dysfunction"), napping status (nap duration), sleep regularity status (nighttime bedtime, morning wake-up time, nighttime sleep duration), and sleep type (morning-type sleep pattern: "morning" type or "morning more than evening" type; night-type sleep pattern: "evening" type or "evening more than morning" type).

Sleep score were constructed by unhealthy sleep factors were defined as: long (> 9h) or short (< 6h) sleep duration, insomnia ("sometimes" or "usually"), snoring disorder ("yes"), night-type sleep pattern ("evening" or "more evening than morning") and excessive daytime sleepiness ("often" or "always "). Each item was scored as 0 (healthy sleep factor) or 1 (unhealthy sleep factor), respectively. Three sleep and circadian pattern categories were defined: good sleep pattern (a score of 0 or 1); moderate sleep pattern (a score of 2 or 3); and bad sleep pattern (a score of 4 or 5).

2.3 Covariates
We included as many potential confounding factors, included sociodemographic data, lifestyle habits, health status, and physiological and biochemical indicators. Sociodemographic data included age (≤ 18 years, 19–40 years and > 40 years), sex (male and female), marital status (married and others), education (no education vs elementary school and above) and occupation was defined as primary occupation before age 60 (no and yes). Lifestyle habits included smoking history, alcohol history, history of passive smoking, tea consumption and whether living alone. Health status variables were body mass index (BMI) (underweight < 18.5 kg/m², normal 18.5–23.9 kg/m², overweight 24-27.9 kg/m², obesity ≥ 28 kg/m²).

2.4 Statistical analysis

First, we investigated differences in baseline data and sleep status between patients with schizophrenia and normal controls. We then used a bar chart to compare the differences in sleep disorders between the case and control groups. We examined covariates between variables and used logistic regression analysis to explore the relationship between sleep status and schizophrenia. A restricted cubic spline was used to examine the expose-response relationship between nocturnal sleep duration and the prevalence of schizophrenia (rms package). Finally, a more comprehensive sleep score was used to assess sleep status, and further logistic regression analysis was used to analyze the relationship between sleep status and schizophrenia. The disease predictive value of sleep scores was assessed using the receiver operating curve (ROC) and its area under the curve (AUC). The above analyses were performed using SPSS 26.0, the R language, MedCalc, and bilateral P < 0.05 was considered statistically significant.

3. Results

3.1 Demographic characteristics

In this study, the majority of participants were young adults, educated, married, employed, non-smokers, non-drinkers, and a greater proportion of those with a body mass index in the normal range of 18.5 ~ 23.9 kg/m². Compared to controls, people with schizophrenia were more likely to be adults aged 19 to 40 years, female, not working, and not married (Table 1).

3.2 Associations of sleep behaviors with schizophrenia

A one-way chi-square test was used to analyze and compare the sleep parameters between the two groups. The results showed that except for sleep disturbance, nap time and sleep type, nighttime sleep duration, sleep latency, sleep efficiency, sleep medication use, whether or not to nap, sleep quality, daytime dysfunction, PSQI score, whether or not to fall asleep regularly, whether or not to wake up regularly, and whether or not to sleep regularly at night in schizophrenia were significantly different from normal controls (P<0.05). The above factors may be risk factors affecting schizophrenia and need further analysis. (Table 2)

From comparing the different types of sleep disturbances, it can be seen from Figure 1 that in the case group, the number of people lacking the energy to do things, frequently feeling sleepy, drugged hypnosis,
having bad dreams, going to the bathroom at night, waking up easily at night and difficulty falling asleep were much higher than in the control group, indicating that sleep disorders are highly prevalent in patients with schizophrenia and are an important factor troubling schizophrenics. (Figure 1)

Covariance analysis was conducted on the factors affecting schizophrenia, and the variance inflation factor (VIF) of each variable was <5, indicating that the independence of these variables did not have serious covariance problems. After adjusting for confounding factors, logistic regression analysis showed that nighttime sleep duration < 6 hours ($OR=2.45$, 95% $CI: 1.67-3.58$), poor sleep quality ($OR=3.26$, 95% $CI: 1.87-5.69$), daytime dysfunction ($OR=3.45$, 95% $CI: 2.44-4.89$), sleep latency >30 min ($OR=2.66$, 95% $CI: 1.88-3.77$), sleep efficiency <85% ($OR=3.31$, 95% $CI: 2.34-4.69$), sleep medication use ($OR=2.68$, 95% $CI: 2.02-3.56$), poor PSQI score ($OR=2.99$, 95% $CI: 2.13-4.21$), irregularity of bedtime ($OR=5.22$, 95% $CI: 3.43-7.93$), waking up irregularly ($OR=4.07$, 95% $CI: 2.67-6.19$), irregular nighttime sleep duration ($OR=5.33$, 95% $CI: 3.59-7.93$), no napping ($OR=1.88$, 95% $CI: 1.34-2.65$) and sometimes napping ($OR=2.06$, 95% $CI: 1.12-3.81$) were risk factors for developing schizophrenia. (Table 3)

The interaction analysis of nighttime sleep duration and sleep quality, naps and nighttime sleep duration was statistically different at $P<0.05$. Interaction analysis showed that sleep patterns with poor sleep quality and less than 6 hours of nighttime sleep was risk factors for developing schizophrenia compared to other sleep patterns. Participants with less than 6 hours of nighttime sleep and no naps was at the highest risk of schizophrenia. (Figure 2 and Figure 3)

We further assessed the relationship between nighttime sleep duration and schizophrenia using restricted cubic spline plots. The results showed that the $OR$ for schizophrenia tended to decrease as the duration of nighttime sleep increased and that short nighttime sleep was a risk factor for developing schizophrenia (Figure 4).

Finally, we performed the construction of sleep scores, and after adjusting for confounding factors, the numerical variables of sleep scores were statistically significant between the two groups, and further analysis led to the conclusion that unfavorable sleep pattern ($OR = 4.19$, 95% $CI: 2.22-7.91$) may be a risk factor for schizophrenia. (Table 4) To assess the value of the application of sleep scores, models with and without sleep scores were fitted. Model 1 included traditional risk factors for schizophrenia, model 2 included the sleep score in model 1 and model 3 included the PSQI score in model 1. There was an improvement in diagnostic power with an $AUC=0.87$ for model 2 compared to model 1, $P=0.005$, and no statistically significant difference compared to model 3, $P=0.969$. (Table 5& Figure 5)

4. Discussion

In this study, we used a case-control study to comprehensively analyze the effects of sleep behaviors on schizophrenia. After adjusting for confounding factors, we found that poor sleep behaviors such as nighttime sleep duration <6 hours, poor sleep quality, irregular waking, falling asleep, and sleep duration, high daytime dysfunction scores, low sleep efficiency, and irregular napping were risk factors for developing schizophrenia. Sleep patterns with less than 6 hours of sleep at night and poor sleep quality,
and sleep patterns with less than 6 hours of sleep at night and no naps are also risk factors for schizophrenia. The optimal sleep pattern was a morning-type sleep pattern with 6-9 hours of nighttime sleep duration, good sleep quality, no daytime sleepiness and no snoring.

Studies have shown that people with schizophrenia are less efficient sleepers, have significantly higher sleep latencies and nocturnal awakenings, and have poorer sleep quality than healthy subjects. Polysomnography studies have shown changes in sleep architecture in patients with schizophrenia compared to healthy controls, with the former exhibiting longer sleep latencies, reduced sleep efficiency, less deep sleep, and more nocturnal awakenings. Typically, healthy control subjects had a sleep latency (SL) of between 10 and 20 minutes, whereas schizophrenics presented with a longer SL (47 minutes), resulting in complaints of insomnia, and schizophrenics self-reported poorer sleep quality than normal subjects. In our findings, sleep disturbances, such as nightmares and easy waking at night, were much more common in people with schizophrenia than in healthy people, and reduced sleep efficiency and difficulty falling asleep were also high risk factors for the development of schizophrenia.

Results from a two-sample, two-way Mendelian randomization study exploring the causality of sleep characteristics and schizophrenia identified morning circadian preference as being associated with a lower risk of schizophrenia, as well as providing clues to the causal relationship between daytime naps, daytime sleepiness and a higher risk of schizophrenia. Several studies have also shown that nocturnal sleep patterns are a high risk factor for developing schizophrenia compared to healthy controls. And the type of sleep at night is usually associated with general mood disorders as well as poorer mood in non-clinical samples. The findings of this study also concur with previous studies that early morning type sleep patterns are better for normal people. Also similar to the results of our study, another studies have concluded that daytime sleepiness and daytime naps may contribute to the development of schizophrenia.

In this study, sleep duration <6 hours at night was a high risk factor for developing schizophrenia, and prolonged sleep was not statistically significant between patients with schizophrenia and normal controls. However, a study suggest that prolonged sleep is associated with a higher risk of schizophrenia and that short periods of sleep are not significantly associated with the risk of schizophrenia. The possible reason is the limitation of the case-control study, such as recall deviation.

The study found that irregular bedtimes, irregular waking times and irregular nighttime sleep schedules, known as irregular circadian rhythms, are risk factors for developing schizophrenia. Previous studies have reached the same conclusion. Recently, it has also been reported that variability in circadian rhythm phenotypes (reduced daily activities; asynchrony with light and dark cycles) during dynamic monitoring at a one-year follow-up is thought to increase the severity of psychotic symptoms and psychosocial impairment in people at high risk for psychosis.

In the management of schizophrenia, a number of behavioral strategies can be implemented to reduce changes in circadian rhythms and to develop good sleep habits. These strategies can include sleep
hygiene training with a focus on regular waking and bedtime, avoiding napping and increasing daytime activity (e.g. physical activity).

Sleep behaviors are multifaceted and often related. Changes in one sleep behavior usually leads to compensatory changes in other sleep behaviors. The highly interrelated nature of various sleep behaviors makes it imperative to approach these factors in an integrated manner. The significance of sleep research in schizophrenia is that sleep problems can be improved, so as to play a certain role in preventing and improving the occurrence and development of schizophrenia. Therefore, this study not only started with the Pittsburgh Sleep Index scale but also added the nap factor, sleep type factor, and sleep regularity factor to it, and assessed it with a more comprehensive sleep assessment model to find the best sleep pattern and provide new ideas for the prevention and treatment of schizophrenia.

This study has the following advantages: it is a more comprehensive assessment of sleep behavior and is not limited to the Pittsburgh Sleep Index scale, but also includes other aspects of sleep factors such as napping status and sleep regularity, and the study analyzes their interaction and uses a more comprehensive sleep score to analyze the study and find the optimal sleep pattern, which provides new ideas to reduce the risk of schizophrenia and has high public health significance and relevance.

This study has some limitations. First, this study used a case-control study, which was weak in verifying causal associations and needs to be validated by other methods, such as cohort studies. Second, participants may be subject to recall bias, leading to overestimation or underestimation of the study results. Finally, the sample size was still small, resulting in a wide range of OR values for some indicators, which may affect the credibility of the study results.

5. Conclusion

Poor sleep behavior is a risk factor for schizophrenia. This study used a more comprehensive sleep score for assessment, the optimal sleep pattern was a morning-type sleep pattern with 6-9 hours of nighttime sleep, good sleep quality, no daytime sleepiness and no snoring. In summary, this study highlights the importance of sleep behaviors in the prevention of schizophrenia. Good sleep behaviors helps to improve the development of schizophrenia and is of great practical importance in preventing and controlling the occurrence of psychiatric system disorders and improving the health of the population.

Declarations

Consent for publication

All participants provided informed consent, including consent to publish scientific manuscripts based on collected data, in order to participate in the study.

Availability of data and materials
The datasets generated and/or analyzed during the current study are not publicly available due to individual privacy but are available in summary/group level form from the corresponding author on reasonable request.

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**Authorship contribution statement**

Yawen Lin, Suping Luo and Zhikai Xiao contributed to the study design, data analysis, and interpretation and drafted the manuscript. Fuhao Zheng, Yihan Liu, Dexiang Ma, Wenping Zhong, Xiaoting Zhou contributed to data analysis and revision of the manuscript. Siying Wu, Shichao Wei and Huangyuan Li contributed to the design of this study, interpretation of data, and critical revision of the manuscript. All authors read and approved the final manuscript.

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**Ethics approval and consent to participate**

All participants joined voluntarily and signed a consent form before participation. The investigation passed the ethics committee of Fujian Provincial Hospital (K2021-04-049).

**Competing interests**

The authors declare that they have no competing interests

**References**


**Figures**
Figure 1

Differences in sleep disturbances in case group and control group (incidence $\geq$3 times per week).
Figure 2

The interaction between sleep quality and nighttime sleep duration in schizophrenia.*

* Using logistics regression to get odds ratio after adjusted age, sex, marital status, occupation, smoking, passive smoking, drinking wine, drinking tea, BMI.
Figure 3

Interaction of nap duration and nighttime sleep duration on schizophrenia. *

* Using logistics regression to get odds ratio after adjusted age, sex, marital status, occupation, smoking, passive smoking, drinking wine, drinking tea, BMI.
Figure 4

Association between nocturnal sleep duration and schizophrenia by unrestricted cubic splines*.

* Using logistics regression to get odds ratio after adjusted age, sex, marital status, occupation, smoking, passive smoking, drinking wine, drinking tea, BMI.
Figure 5

ROC curves for models with and without sleep scores *

* Model 1: adjusted for age, sex, marital status, occupation, drinking wine, drinking tea, smoking, passive smoking, BMI. Model 2: as model 1, adjusted sleep mode score. Model 3: as model 1, adjusted PSQI score.