

# Variations in Sleep Architecture among Different Subtypes of Schizophrenia: A Cross-sectional Study

SAGARIKA RAY<sup>1</sup>, PARTHA SARATHI KUNDU<sup>2</sup>, AMIT KUMAR BHATTACHARYA<sup>3</sup>, AMIT KUMAR PAL<sup>4</sup>

## ABSTRACT

**Introduction:** Schizophrenia is a severe mental disorder characterised by positive symptoms such as delusions and hallucinations, as well as negative symptoms including anhedonia, asociality, avolition, and affective blunting. It may also be associated with cognitive deficits. Sleep disturbances are commonly encountered in schizophrenia, and there may be variations in sleep patterns among its different subtypes. These differences in sleep patterns could have prognostic implications for the various subtypes of schizophrenia. Effective management of sleep disturbances could contribute to the recovery and well-being of individuals diagnosed with schizophrenia.

**Aim:** To compare the differences in sleep architecture between the various subtypes of schizophrenia and to compare them with socio-demographically matched healthy volunteers.

**Materials and Methods:** A cross-sectional study was conducted at the Institute of Psychiatry-Centre of Excellence, Kolkata, West Bengal, India over a duration of one year (May 2016 to June 2017). The study included 60 medication-naïve patients diagnosed with schizophrenia according to International Classification of Diseases (ICD)-10 criteria, and a control group of 30 demographically matched healthy volunteers. All study participants were aged between 18 and 60 years and free from any co-morbid illnesses. Patients with schizophrenia were further classified into four groups based on the ICD-10 subtypes: paranoid, hebephrenic, catatonic, and undifferentiated. Overnight polysomnography was performed to assess sleep parameters, including total record time, total sleep time, sleep onset latency, Rapid Eye Movement (REM), sleep latency, sleep

efficiency, durations of Total Non Rapid Eye Movement (NREM) Sleep, Total REM sleep, and the different phases of NREM sleep. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20.0. Analysis of Variance (ANOVA), Chi-square, and t-test were used as applicable, with a p-value <0.05 considered statistically significant.

**Results:** The results showed a decrease in sleep efficiency, total sleep time, and shorter duration of mean N1, N2, and N3 sleep in schizophrenia patients compared to the control group. There was a significant difference in N3 sleep duration, reduced duration of total NREM and REM sleep, reduced REM latency, increased sleep onset latency, and the number of awakenings during sleep in schizophrenia patients. Statistically significant differences (p-values <0.05) were also noted in some sleep parameters among the various subtypes of schizophrenia. The paranoid subtype had the shortest REM latency, while the catatonic subtype had the longest. The hebephrenic subtype had the lowest percentage of REM sleep and sleep efficiency, while the catatonic subtype had the highest. The duration of Slow Wave Sleep (SWS) was lowest in the undifferentiated subtype and highest in the catatonic subtype.

**Conclusion:** This study reveals significant differences in sleep patterns between patients with schizophrenia and the control group, as well as among the various subtypes of schizophrenia. These distinctions provide insight into the relationship between schizophrenia subtypes, sleep irregularities, and clinical consequences. Further investigation is necessary to explore differences in sleep architecture among the various subtypes of schizophrenia and yield clinically meaningful results.

**Keywords:** Catatonic, Hebephrenic, Paranoid, Polysomnography

## INTRODUCTION

Schizophrenia is a major psychiatric disorder that imposes a significant disease burden on individuals and society in terms of morbidity and medical expenditure worldwide [1]. Clinically, individuals with schizophrenia may exhibit positive symptoms (such as hallucinations and delusions) and negative symptoms (such as social withdrawal, anhedonia, and apathy), along with various cognitive impairments. Although sleep disturbances and sleep-related co-morbidities are highly prevalent in schizophrenia and consistently reported across chronic, early-course, and first-episode cases, they are not considered diagnostic criteria. However, severe sleep disturbance in schizophrenia may require independent clinical attention, as up to 80% of patients with schizophrenia experience such symptoms [2,3]. This has led to significant research efforts to understand the relationship between disrupted sleep and schizophrenia.

The sleep-wakefulness cycle can be objectively assessed through polysomnography, which quantitatively measures three basic parameters: the electroencephalogram (EEG), the electrooculogram

(EOG), and the electromyogram (EMG) [4]. The Rechtschaffen and Kales (1968) system for scoring the sleep-wake cycle distinguishes a waking state, NREM sleep, and REM sleep. NREM sleep is further divided into four stages: a) Stage 1 sleep is characterised electrophysiologically by relatively low-voltage theta waves; b) Stage 2 sleep is defined by the presence of sleep spindles and K complexes; and c) Stage 3 and 4 sleep are characterised by the presence of slow, high-amplitude delta waves [5]. The American Academy of Sleep Medicine (AASM) modified the classification and subdivided NREM sleep into three stages: N1, N2, and N3, with N3 reflecting SWS, combining Stage 3 and 4 of NREM sleep [6].

Studies have demonstrated a bidirectional relationship between sleep deprivation and psychotic symptoms, where sleep disturbances can be caused by psychotic experiences, and at the same time, sleep problems can induce or worsen the occurrence of psychotic symptoms [7,8]. A strong association between sleep insufficiency and specific prodromal symptoms (such as suspiciousness and perceptual abnormalities) has recently been established in a large sample of youths at a clinically high-risk for psychosis [9]. Sleep

impairment in schizophrenia is also associated with poor clinical outcomes, including suicidal ideation, lifetime suicide attempts, hallucinations, elevated paranoia, and overall deteriorated socio-occupational functioning [10,11]. Experimental manipulation of sleep through sleep restriction or deprivation can lead to perceptual distortions and paranoia in non clinical populations [12,13]. Recent EEG studies have focused on alterations in sleep-specific rhythms such as sleep spindles and slow waves, revealing dysfunctions in neural and molecular mechanisms in both chronic and early-phase schizophrenia [14]. Sleep disturbances in schizophrenia are closely linked to clinical symptoms and cognitive impairments, involving thalamocortical circuits, calcium channels, and gamma-aminobutyric acid (GABA)-glutamate neurotransmission. The relationship between sleep dysfunction and the clinical features of schizophrenia warrants evaluation as a potential biomarker with prospects for novel treatment interventions [15,16].

While there is existing literature on sleep architectural differences in schizophrenia compared to healthy controls, there is a lack of research exploring sleep differences among the various subtypes of schizophrenia. This study aims to shed light on this topic, particularly in the Indian context. The objective of this study was to compare the sleep architecture, as evidenced by polysomnographic findings, among the various subtypes of schizophrenia and also in comparison to socio-demographically matched healthy volunteers, referred to as the control group.

## MATERIALS AND METHODS

The present study was a hospital-based cross-sectional study that includes 60 cases diagnosed with schizophrenia and 30 healthy volunteers serving as a comparison group, referred to as "controls". The study was conducted over a duration of one year (May 2016 to June 2017) at the Institute of Psychiatry-Centre of Excellence, IPGME&R, Kolkata, West Bengal, India. The study was conducted on patients attending the inpatient and outpatient services at the Institute of Psychiatry. The study was conducted after obtaining the necessary clearance from the Institutional Ethical Committee of IPGME&R, Kolkata (Memo No. Inst/IEC/2016/242). Informed consent was obtained from all participants, and a detailed information sheet was provided to them in their preferred language (either their mother tongue or English).

### Inclusion criteria:

#### a. Cases

1. Patients diagnosed with schizophrenia according to the ICD-10 criteria [17] and confirmed separately by two different clinicians.
2. Patients who have never taken any antipsychotic medications.
3. Patients who were not violent or at risk of harming themselves or others.
4. Age between 18-60 years.

#### b. Control group (comparison group):

1. Healthy attendants of patients who are not their blood relatives.
2. Age between 18-60 years.
3. Not currently presenting with symptoms related to any psychiatric illness, which was further confirmed by the absence of significant abnormalities in the detailed mental status examination conducted independently by two clinicians.

### Exclusion criteria:

#### a. Cases

1. Patients with psychiatric co-morbidities such as mood disorders, substance use disorders, obsessive-

compulsive disorder, dementia, schizoaffective disorder, and mental retardation.

2. Patients suffering from any co-morbid medical illnesses such as seizures, stroke, neurodegenerative diseases like Parkinson's disease, cardiovascular disorders, metabolic syndrome, respiratory disorders, and sleep apnoea.
  3. Patients with schizophrenia who had a prior history of, or are currently taking, psychiatric medications.
- b. Controls group (comparison group):
1. Presence of any past psychiatric illness.
  2. Family history of psychiatric illness in a first-degree relative.
  3. History of substance use.
  4. Other major medical or surgical illnesses, including sleep apnoea.

**Sampling technique:** Convenience sampling of eligible participants attending the psychiatry outpatient department was performed until the required sample size was achieved.

**Sample size:** The sample size was calculated using the formula  $n = z^2 pq / d^2$ , where:

$Z = 1.96$  corresponding to a significance level of 0.05 and confidence level of 0.95 or 95%,  $p = 0.80$ , the prevalence of upto 80% sleep-related disturbances among patients with Schizophrenia [2,3],  $q = 1 - p = 0.20$  and  $d = \text{absolute precision} = 0.01$  with 10% absolute precision. Based on these parameters, the calculated sample size was 61.

Informed consent was obtained from 82 patients with Schizophrenia and 45 healthy volunteers. Twenty patients were admitted to IOP-COE, Kolkata for indoor polysomnography assessment. For the remaining 62 cases and 45 healthy volunteers, appointments were given for polysomnography about one week after their initial visit. However, only 40 non-admitted cases and 30 healthy volunteers actually attended their scheduled polysomnography assessment. A total of 60 drug-naïve patients, 31 females and 29 males, who met the ICD-10 diagnostic criteria for schizophrenia, were recruited for the study [17]. Healthy volunteers, totaling 30 individuals comprising 15 females and 15 males, with similar socio-demographic characteristics were also recruited to serve as a comparison group, termed as the control group in this study.

**Detailed methodology:** After recruiting cases and controls, the cases were further subclassified into paranoid, catatonic, hebephrenic, and undifferentiated schizophrenia based on the ICD 10 diagnostic criteria [17]. Consequently, they were divided into four groups: catatonic schizophrenia (three cases), paranoid Schizophrenia (44 cases), hebephrenic schizophrenia (three cases), and undifferentiated schizophrenia (10 cases) [17].

A comprehensive history was obtained from the selected patients, including their socio-demographic profile, chief complaints, history of present illness, treatment history, past medical history, family history, and personal history, including any history of substance use.

Overnight polysomnography was conducted on all the cases and controls at the Department's Sleep Laboratory using the "Philips Respironics, Model Alice 6" instrument, powered by Sleepware G3 software with an integrated somnolyser scoring system. Ten EEG electrodes (Fp1, Fp2, F7, F8, C3, C4, T3, T4, O1, and O2) were applied to the scalp based on the 10-20 system. Additionally, two EOG electrodes were placed, one 1 cm below the left outer cantus and one 1 cm above the right outer cantus. Three surface EMG electrodes were applied over the chin muscles [4]. The recording duration targeted for all study participants was eight hours.

**Sleep architecture parameters:** The sleep architecture parameters studied were as follows:

- **Total sleep time:** The duration of the recording when the person is actually asleep.
- **Total wake time:** The duration of the recording when the person is lying in bed and awake.
- **Total record time:** The total duration of the polysomnographic recording, including both sleep time and wake time, from lights off until the recording is stopped.
- **Sleep onset latency:** The duration from the start of the recording (lights off) until the person falls asleep or enters the NREM stage of sleep.
- Number of awakenings during sleep.
- **Sleep efficiency:** The total sleep time expressed as a percentage of the total record time.
- **REM sleep latency:** The time elapsed between sleep onset and the first REM period.
- Duration of REM sleep.
- Duration of NREM sleep.
- **Percentage of slow-wave sleep (SWS):** The duration of slow wave or N3 sleep expressed as a percentage of total sleep time.
- **Duration of sleep in N1, N2, and N3 phases:** The durations of the three phases of NREM sleep.
- Duration of the first REM period [18].

The objective of this study was to assess whether significant differences exist in sleep parameters among the various subtypes of schizophrenia, as well as in comparison to healthy individuals. Initially, the means of these sleep variables were compared between the four subgroups of schizophrenia and healthy controls to determine if there were any significant differences. Subsequently, the means specifically related to the four subtypes of schizophrenia were assessed for significance.

The primary outcome of this study was to evaluate whether sleep variables can serve as potential biomarkers to aid in the diagnosis of schizophrenia and its subtypes. Additionally, the study aims to investigate any clinical and prognostic implications of such differences. The findings could inform targeted interventions to mitigate sleep disturbances in patients with schizophrenia, potentially reducing the severity of symptoms and improving their quality of life. This, in turn, could help alleviate the burden of the disease on the community.

As a secondary outcome, the study aims to provide insights into whether sleep parameters can serve as trait markers for the various subtypes of schizophrenia.

## STATISTICAL ANALYSIS

The data were entered into a Microsoft Excel spreadsheet and analysed using the SPSS package, version 20.0. Student's independent samples t-test was utilised to compare normally distributed numerical variables between groups. Unpaired proportions were compared using the Chi-square test. A p-value of  $\leq 0.05$  was considered statistically significant. Significance was initially assessed by performing an ANOVA test among all five groups in this study, which included the four subtypes of schizophrenia and the control group. Subsequently, an additional ANOVA test was conducted specifically among the four subtype groups.

## RESULTS

Cases and control group were age and sex-matched, showing no statistically significant difference in the distribution of mean age ( $p$ -value $\leq 0.38$ ) and gender ( $p$ -value $\leq 0.88$ ) [Table/Fig-1].

Group	Male	Female	Mean age (in years)
Case	29 (48.3%)	31 (51.7%)	31.58 $\pm$ 11.69
Control	15 (50%)	15 (50%)	33.67 $\pm$ 8.13
p-value*	0.88		0.38

**[Table/Fig-1]:** Distribution of gender and mean age (in years) among cases and controls.

\*p-value  $< 0.05$  considered to be significant

The total record time and total sleep time, regardless of the subtype of schizophrenia, were significantly lower than those in the control group. Among the subtypes, the undifferentiated subtype had the shortest total record time, while the paranoid subtype had the longest. The hebephrenic subtype had the shortest total sleep time, while the catatonic subtype had the longest. Sleep onset latency was significantly increased in schizophrenia compared to controls, with the highest increase was observed in the paranoid subtype, followed by the hebephrenic and undifferentiated subtypes, and the shortest increase in the catatonic subtype. However, the differences in these three parameters were not statistically significant ( $p$ -value=0.0834, 0.224, and 0.138 for total record time, total sleep time, and sleep onset latency, respectively) among the various subtypes of schizophrenia. Notably, the latency to the onset of the first REM sleep period was significantly shorter in schizophrenia compared to controls, with the shortest REM latency observed in the paranoid subtype and the longest in the catatonic subtype. This difference was also statistically significant among the various subtypes of schizophrenia, as shown in [Table/Fig-2].

Sleep efficiency was decreased in schizophrenia, with the lowest efficiency observed in the hebephrenic subtype and the highest in the catatonic subtype. The difference in mean sleep efficiency among the various subtypes of schizophrenia was also statistically significant ( $p$ -value $\leq 0.001$ ). The mean number of awakenings during sleep was significantly increased in schizophrenia, with the highest number of awakenings in the hebephrenic subtype and the least in the catatonic subtype. This difference was also significant among the various subtypes of schizophrenia, as shown in [Table/Fig-3].

The durations of mean N1, N2, and N3 sleep were found to be decreased in schizophrenia compared to controls. While the difference between cases and controls was not statistically significant for N1 and N2, a significant difference ( $p$ -value $\leq 0.0001$ ) was observed for N3 (SWS). This difference was also found to be statistically significant among the various subtypes of schizophrenia. The mean durations of both total NREM and REM sleep were decreased in schizophrenia compared to controls. The lowest percentage of NREM sleep duration was observed in the catatonic subtype, while the highest percentage was seen in the hebephrenic subtype. The lowest percentage of REM sleep duration was observed in the hebephrenic subtype, while the highest percentage was seen in the catatonic subtype. Statistically significant differences ( $p$ -value $\leq 0.0001$ ) in the percentages of total REM and total NREM sleep were found among the various subtypes of schizophrenia. The duration of the mean first REM period was significantly decreased in schizophrenia compared to controls, with the shortest duration observed in the hebephrenic subtype and the longest duration in the catatonic subtype. The difference in the mean duration of the first REM period among the various subtypes of schizophrenia was also statistically significant ( $p$ -value $\leq 0.0001$ ), as shown in [Table/Fig-3,4].

## DISCUSSION

Schizophrenia is a chronic mental disorder that significantly contributes to the global burden of disease [1]. The incidence, prevalence, and Disability Adjusted Life Years (DALYs) related to Schizophrenia have been found to increase worldwide between

Sleep variable	Subtypes	Mean±Standard Deviation	Minimum	Maximum	p-value* among all the five groups (including the control group)	p-value* and f value among the four subtypes only
Total record time (In minutes)	Catatonic n=3	384.66±13.05	371.00	397.00	<0.0001	p-value=0.0834 f-value=0.2885
	Hebephrenic n=3	384.66±11.84	371.00	392.00		
	Paranoid n=44	394.77±41.98	300.00	468.00		
	Undifferentiated n=10	384.50±17.44	354.00	407.00		
	Control n=30	461.33±13.77	428.00	478.00		
Total sleep time (In minutes)	Catatonic n=3	300.33±12.58	287.00	312.00	<0.0001	p-value=0.224 f-value=1.5001
	Hebephrenic n=3	226.33±7.23	218.00	231.00		
	Paranoid n=44	281.02±52.74	194.00	398.00		
	Undifferentiated n=10	275.40±20.94	237.00	302.00		
	Control n=30	421.93±17.67	374.00	446.00		
Sleep latency (In minutes)	Catatonic n=3	30.00±2.00	28.00	32.00	<0.0001	p-value=0.138 f-value=1.912
	Hebephrenic n=3	42.66±10.78	35.00	55.00		
	Paranoid n=44	43.97±10.87	23.00	64.00		
	Undifferentiated n=10	41.40±5.37	35.00	51.00		
	Control n=30	19.00±5.05	8.00	29.00		
Mean REM latency (In minutes)	Catatonic n=3	70.66±1.52	69.00	72.00	<0.0001	p-value=<0.0001 f-value=8.6715
	Hebephrenic n=3	46.33±9.01	37.00	55.00		
	Paranoid n=44	43.63±9.72	28.00	65.00		
	Undifferentiated n=10	48.80±6.57	41.00	64.00		
	Control n=30	80.70±5.97	70.00	91.00		

**[Table/Fig-2]:** Comparison of the total record time, total sleep time, mean sleep latency and the mean REM latency between the various subtypes of Schizophrenia and controls. \*p-value <0.05 considered to be significant. ANOVA tests have been used here

Sleep variable	Subtypes	Mean±Standard Deviation	Minimum	Maximum	p-value* among all the five groups (including the control group)	p-value* and f value among the 4 subtypes only
Mean sleep efficiency (In percentages)	Catatonic n=3	78.06±0.63	77.36	78.59	<0.0001	p-value=<0.001 f-value=6.5628
	Hebephrenic n=3	58.83±0.08	58.76	58.93		
	Paranoid n=44	70.66±6.10	60.89	85.59		
	Undifferentiated n=10	71.50±2.96	66.94	76.26		
	Control n=30	91.43±1.86	86.57	95.07		
Mean number of awakenings	Catatonic n=3	2.00±1.00	1.00	3.00	<0.0001	p-value =<0.001 f-value=4.0299
	Hebephrenic n=3	6.33±1.52	5.00	8.00		
	Paranoid n=44	4.18±1.63	1.00	7.00		
	Undifferentiated n=10	4.20±0.91	3.00	6.00		
	Control n=30	0.23±0.43	0.00	1.00		
Mean N1 (In minutes)	Catatonic n=3	29.66±1.52	28.00	31.00	0.1633	p-value=0.129 f-value=1.97
	Hebephrenic n=3	23.33±2.08	21.00	25.00		
	Paranoid n=44	31.38±6.38	22.00	39.00		
	Undifferentiated n=10	29.90±2.68	26.00	34.00		
	Control n=30	35.30±2.35	32.00	38.00		
Mean N2 (In minutes)	Catatonic n=3	171.66±8.50	163.00	180.00	0.1613	p-value=0.963 f-value=0.0934
	Hebephrenic n=3	169.33±2.88	165.00	174.00		
	Paranoid n=44	174.97±26.51	136.00	202.00		
	Undifferentiated n=10	176.70±10.04	167.00	195.00		
	Control n=30	180.70±14.06	157.00	210.00		

**[Table/Fig-3]:** Comparison between the mean sleep efficiency, mean number of awakenings, mean N1, and mean N2 between the subtypes of Schizophrenia and controls. \*p-value <0.05 considered to be significant. ANOVA tests have been used here

Sleep variable	Subtypes	Mean±Standard Deviation	Minimum	Maximum	p-value* among all the 5 groups (including the control group)	p-value* and f value among the 4 subtypes only
Mean N3 (In minutes)	Catatonic n=3	45.00±1.00	44.00	46.00	<0.0001	p-value=<0.0001 f-value=4.9023
	Hebephrenic n=3	25.66±1.52	22.00	25.00		
	Paranoid n=44	24.97±10.21	13.00	44.00		
	Undifferentiated n=10	22.50±5.12	17.00	30.00		
	Control n=30	100.13±5.93	89.00	110.00		

<b>Mean NREM (In percentage)</b>	Catatonic n=3	82.01±0.12	81.88	82.12	<0.0001	p-value=<0.0001 f-value=7.8365
	Hebephrenic n=3	89.85±0.17	89.60	90.00		
	Paranoid n=44	88.35±2.53	83.78	92.78		
	Undifferentiated n=10	88.81±1.73	85.57	91.14		
	Control n=30	76.56±1.79	73.93	79.90		
<b>Mean REM (In percentage)</b>	Catatonic n=3	17.98±0.12	17.8800	18.12	<0.0001	p-value=<0.0001 f-value=7.8228
	Hebephrenic n=3	10.14±0.17	10.00	10.34		
	Paranoid n=44	11.64±2.54	7.22	16.22		
	Undifferentiated n=10	11.18±1.73	8.86	14.43		
	Control n=30	23.43±1.79	20.10	26.07		
<b>Mean first REM period (In minutes)</b>	Catatonic n=3	13.00±0	13.00	13.00	<0.0001	p-value=<0.0001 f-value=17.3651
	Hebephrenic n=3	4.33±0.57	4.00	5.00		
	Paranoid n=44	6.06±1.87	3.00	10.00		
	Undifferentiated n=10	6.60±0.96	5.00	8.00		
	Control n=30	17.83±2.13	15.00	24.00		

**[Table/Fig-4]:** Comparison of the mean N3, NREM, REM, and the first REM period between the Sub-types of Schizophrenia and controls.

\*p-value <0.05 considered to be significant. ANOVA tests have been used here

1990 and 2019 [19]. Sleep disturbances are commonly experienced by individuals diagnosed with schizophrenia [2,3]. There is evidence that sleep disturbances, especially insomnia, often precede the onset of overt psychotic symptoms in schizophrenia or may be associated with acute exacerbations of the disorder [14,20]. Literature reports alterations in sleep architecture in schizophrenia, including deficits in SWS, decreased REM latency, increased sleep onset latency, decreased total sleep time, and decreased sleep efficiency [14].

Schizophrenia has been classified into various subtypes based on specific clinical characteristics according to the ICD-10 classification [17]. The validity of this subtyping system has been supported by a literature review conducted by McGlashan TH and Fenton WS [21]. These subtypes may have prognostic implications, with paranoid schizophrenia showing a higher chance of recovery and better long-term outcomes. The hebephrenic variant is associated with a poor prognosis, while the undifferentiated subtype tends to have a chronic but stable deficit [22]. This study aims to evaluate the differences in sleep architecture among the different subtypes of schizophrenia. Such differences may serve as trait markers for the various subtypes of schizophrenia, which could have potential clinical implications in predicting the onset of illness in individuals at high risk of developing psychosis. Additionally, these differences may have prognostic implications, and treatment strategies targeting sleep disturbances could potentially aid in the recovery process. Therefore, it is important to study newer interventions, both pharmacological and non-pharmacological, to improve the overall quality of life for individuals living with schizophrenia [14].

The present study demonstrates a decrease in sleep efficiency, total sleep time, shorter duration of mean N1, N2, and N3 sleep, with a significant difference in SWS duration. There is also a reduced duration of total NREM and REM sleep, reduced REM latency, an increase in sleep onset latency, and an increase in the number of awakenings during sleep in schizophrenia compared to healthy controls. Statistically significant differences in sleep parameters were noted for some of the variables among the various subtypes of schizophrenia. REM latency was decreased the most in the paranoid subtype and was longest in the catatonic subtype. The percentage of REM sleep and sleep efficiency were found to be lowest in the hebephrenic subtype and highest in the catatonic subtype. The duration of SWS or N3 sleep was reduced the most in the undifferentiated subtype, and the highest duration was recorded in the catatonic subtype.

The findings of this study were consistent with those of the meta-analysis by Chan MS et al., who reported a decrease in total sleep

time, sleep efficiency, REM latency, duration of REM sleep and SWS, with an increase in sleep onset latency and total awake time after sleep onset in patients with schizophrenia [23]. Several studies were evaluated that revealed patients with schizophrenia showed significantly lower total sleep time and sleep efficiency, longer sleep onset latency and total awake time, increased N1, reduced N3 (SWS) and REM sleep, shorter REM latency, and increased REM density compared to healthy controls. With the progression of the illness, REM latency tends to normalise, but deficits in SWS become more evident [24-35].

Sleep patterns in schizophrenia undergo changes after treatment with antipsychotic drugs, as observed in some studies [24, 25]. A study by Monti JM and Monti D showed a significant increase in total sleep time, along with an increase in N2 sleep and SWS, after patients with schizophrenia were treated with atypical or second-generation antipsychotic drugs such as olanzapine, risperidone, and clozapine. When schizophrenia patients were treated with first-generation or typical antipsychotics like haloperidol and flupenthixol, a decrease in sleep latency and an increase in sleep efficiency were noted [24]. Another study by Kluge M et al., compared the effects of olanzapine and clozapine on modifying the sleep architecture in patients with schizophrenia. Both of these drugs increased the total sleep time and sleep efficiency while decreasing the sleep onset latency. Olanzapine was observed to increase REM sleep and SWS, while there was a slight decrease in SWS with an increase in N2 sleep in patients treated with clozapine [25].

Reports regarding REM sleep duration are controversial, with a study by Lauer CJ et al., stating that there is no appreciable difference in REM sleep between schizophrenia and controls [31]. However, a study by Sarkar S et al., states that there is an increase in the percentage of REM sleep with increasing positive symptoms [36]. In this study, it has been observed that there is a decrease in REM sleep duration in schizophrenia patients compared to healthy controls, which was in line with the findings of Chan MS et al., who reported a decrease in REM sleep duration in schizophrenia, and Poulin J et al., who reported that REM sleep duration progressively decreases with an increase in psychotic symptoms of schizophrenia [23, 37]. The duration of the first REM period has been found to decrease in schizophrenia, confirming the findings of Ilanković A et al., and Keshavan MS et al., [26, 28]. Yetkin S et al., found a decrease in the percentage of REM sleep in patients with schizophrenia compared to controls, with similar findings obtained in this study [29]. SWS deficits have been observed in schizophrenia [38]. These deficits have been correlated with negative symptoms, cognitive impairment, and reduced ventricular size [33, 39-42]. There is a dearth of literature regarding differences

in sleep patterns among the different subtypes of schizophrenia, and further research is warranted in this regard to generate clinically meaningful results. Very few studies are available that compare the differences in polysomnographic findings among the various subtypes of schizophrenia. More work needs to be done with a larger sample size, including a comparable number of cases representing each subtype, to accurately ascertain the differences in sleep parameters in patients with schizophrenia. Longitudinal studies may be undertaken to examine if there are differences in sleep parameters after treatment with antipsychotic drugs and whether such differences are similar in the case of treatment with conventional and atypical antipsychotics. There is a wide scope for research to unravel whether the various sleep parameters can serve as trait markers of the different subtypes of schizophrenia, which might have potential prognostic implications and may predict treatment outcomes. Further research with a greater number of study participants from each subtype of schizophrenia needs to be performed to generate clinically meaningful results regarding whether the sleep architecture variables can serve as trait markers of the various subtypes of schizophrenia, justifying the need to retain these subtypes in the newer classification systems.

### Limitation(s)

Methodological shortcomings have limited the validity of this study. These shortcomings include a small number of subjects, as it is very difficult to obtain polysomnography data in drug-naive patients during the acute phase of the illness, particularly in the case of catatonic and hebephrenic subgroups. Furthermore, there was inadvertent heterogeneity of subjects due to the difficulty of consistently categorising patients into subgroups (paranoid, catatonic, hebephrenic, and undifferentiated) or confirming that patients were in similar phases of the clinical course (acute, subacute, chronic). Additionally, convenience sampling was utilised due to time constraints.

### CONCLUSION(S)

This comparative cross-sectional study highlights the significant variations in sleep architecture among different subtypes of schizophrenia. Understanding these differences can contribute to a more nuanced comprehension of the relationship between schizophrenia subtypes, sleep disturbances, and clinical outcomes. Further research is warranted to elucidate the underlying mechanisms and potential interventions to ameliorate sleep disturbances in individuals with schizophrenia.

### Acknowledgements

Authors extend their heartfelt appreciation to the participants of this study and the technical staff, whose active involvement has been the cornerstone of its success. Authors also acknowledge the immense support from the competent authorities for allowing access to the necessary equipment. Lastly, but not least, authors would like to convey their deep gratitude to the faculty members whose guidance, encouragement, and unwavering support have been instrumental in shaping this study.

### REFERENCES

- [1] Charlson FJ, Ferrari AJ, Santomauro DF, Diminic S, Stockings E, Scott JG, et al. Global epidemiology and burden of schizophrenia: Findings from the global burden of disease study 2016. *Schizophr Bull.* 2018;44(6):1195-203.
- [2] Waite F, Myers E, Harvey AG, Espie CA, Startup H, Sheaves B, et al. Treating sleep problems in patients with schizophrenia. *Behav Cogn Psychother.* 2016;44(3):273-87.
- [3] Cohrs S. Sleep disturbances in patients with Schizophrenia: Impact and effect of antipsychotics. *CNS Drugs.* 2008;22(11):939-62.
- [4] Markun LC, Sampat A. Clinician-focused overview and developments in polysomnography. *Curr Sleep Med Rep.* 2020;6(4):309-21.
- [5] Rechtschaffen A, Kales A. A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. Issue 204 of NIH publication. Los Angeles: U. S. National Institute of Neurological Diseases and Blindness, Neurological Information Network; 1968.

- [6] Iber C, Ancoli-Israel S, Chesson AL, Quan SF. The AASM manual for the scoring of sleep and associated events: Rules, terminology, and technical specification, 1<sup>st</sup> ed. Westchester, Illinois: American Academy of Sleep Medicine; 2007.
- [7] Chiu VW, Ree M, Janca A, Waters F. Sleep in schizophrenia: Exploring subjective experiences of sleep problems, and implications for treatment. *Psychiatr Q.* 2016;87(4):633-48.
- [8] Waite F, Evans N, Myers E, Startup H, Lister R, Harvey AG, et al. The patient experience of sleep problems and their treatment in the context of current delusions and hallucinations. *Psychol Psychother.* 2016;89(2):181-93.
- [9] Goines KB, LoPilato AM, Addington J, Bearden CE, Cadenhead KS, Cannon TD et al. Sleep problems and attenuated psychotic symptoms in youth at clinical high-risk for psychosis. *Psychiatry Res.* 2019;282:112492.
- [10] Subramaniam M, Abidin E, Shahwan S, Satghare P, Vaingankar JA, Rama Sendren J, et al. Prevalence, correlates and outcomes of insomnia in patients with first episode psychosis from a tertiary psychiatric institution in Singapore. *Gen Hosp Psychiatry.* 2018;51:15-21.
- [11] Miller BJ, Parker CB, Rapaport MH, Buckley PF, McCall WV. Insomnia and suicidal ideation in nonaffective psychosis. *Sleep.* 2019;42(2):zsy215.
- [12] Reeve S, Emsley R, Sheaves B, Freeman D. Disrupting sleep: The effects of sleep loss on psychotic experiences tested in an experimental study with mediation analysis. *Schizophr Bull.* 2018;44(3):662-71.
- [13] Kumari V, Ettinger U. Controlled sleep deprivation as an experimental medicine model of schizophrenia: An update. *Schizophr Res.* 2020;221:04-11.
- [14] Ferrarelli F. Sleep abnormalities in schizophrenia: State of the art and next steps. *Am J Psychiatry.* 2021;178(10):903-13.
- [15] Ferrarelli F, Peterson MJ, Sarasso S, Riedner BA, Murphy MJ, Benca RM, et al. Thalamic dysfunction in schizophrenia suggested by whole-night deficits in slow and fast spindles. *Am J Psychiatry.* 2010;167(11):1339-48.
- [16] Manoach DS, Pan JQ, Purcell SM, Stickgold R. Reduced sleep spindles in schizophrenia: A treatable endophenotype that links risk genes to impaired cognition? *Biol Psychiatry.* 2016;80(8):599-608.
- [17] The ICD-10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. Geneva. World Health organization. 1992.
- [18] Boulos MI, Jairam T, Kendzerska T, Im J, Mekhael A, Murray BJ. Normal polysomnography parameters in healthy adults: A systematic review and meta-analysis. *Lancet Respir Med.* 2019;7(6):533-43.
- [19] Solmi M, Seitidis G, Mavridis D, Correll CU, Dragioti E, Guimond S, et al. Incidence, prevalence, and global burden of schizophrenia-data, with critical appraisal, from the Global Burden of Disease (GBD) 2019. *Mol Psychiatry.* 2023.
- [20] Kaskie RE, Graziano B, Ferrarelli F. Schizophrenia and sleep disorders: Links, risks, and management challenges. *Nat Sci Sleep.* 2017;9:227-39.
- [21] McGlashan TH, Fenton WS. Classical Subtypes for schizophrenia: Literature review for DSM-IV. *Schizophrenia Bulletin.* 1991;17(4):609-32.
- [22] Fenton WS, McGlashan TH. Natural history of schizophrenia subtypes: I. longitudinal study of paranoid, hebephrenic, and undifferentiated Schizophrenia. *Arch Gen Psychiatry.* 1991;48(11):969-77.
- [23] Chan MS, Chung KF, Yung KP, Yeung WF. Sleep in schizophrenia: A systematic review and meta-analysis of polysomnographic findings in case-control studies. *Sleep Med Rev.* 2017;32:69-84.
- [24] Monti JM, Monti D. Sleep in schizophrenia patients and the effects of antipsychotic drugs. *Sleep Med Rev.* 2004;8(2):133-48.
- [25] Kluge M, Schacht A, Himmerich H, Rummel-Kluge C, Wehmeier PM, Dalal M, et al. Olanzapine and clozapine differently affect sleep in patients with schizophrenia: Results from a double-blind, polysomnographic study and review of the literature. *Schizophr Res.* 2014;152(1):255-60.
- [26] Ilanković A, Damjanović A, Ilanković V, Filipović B, Janković S, Ilanković N. Polysomnographic sleep patterns in depressive, schizophrenic and healthy subjects. *Psychiatr Danub.* 2014;26(1):20-26.
- [27] Keshavan MS, Reynolds CF, Kupfer DJ. Electroencephalographic sleep in schizophrenia: A critical review. *Compr Psychiatry.* 1990;31(1):34-47.
- [28] Keshavan MS, Reynolds CF 3<sup>rd</sup>, Miewald MJ, Montrose DM, Sweeney JA, Vasko RC Jr et al. Delta sleep deficits in schizophrenia: Evidence from automated analyses of sleep data. *Arch Gen Psychiatry.* 1998;55(5):443-48.
- [29] Yetkin S, Aydin H, Özgen F, Sütçüoğlu L, Bozkurt A. Sleep architecture in schizophrenia patients. *Türk Psikiyatri Derg [Turkish Journal of Psychiatry].* 2011;22(1):01-09. Turkish.
- [30] Jus K, Bouchard M, Jus AK, Villeneuve A, Lachance R. Sleep eeg studies in untreated, long-term schizophrenic patients. *Arch Gen Psychiatry.* 1973;29(3):386-90.
- [31] Lauer CJ, Schreiber W, Pollmächer T, Holsboer F, Krieg JC. Sleep in schizophrenia: A polysomnographic study on drug-naive patients. *Neuropsychopharmacology.* 1997;16(1):51-60.
- [32] Afonso P, Figueira ML, Paiva T. Sleep wake patterns in Schizophrenia patients compared to healthy controls. *The World J Biological Psychiatry.* 2014;15(7):517-24.
- [33] Yang C, Winkelman JW. Clinical significance of sleep EEG abnormalities in chronic schizophrenia. *Schizophr Res.* 2006;82(2-3):251-60.
- [34] Tandon R, Shipley JE, Eiser AS, Greden JF. Association between abnormal REM sleep and negative symptoms in schizophrenia. *Psychiatry Res.* 1989;27(3):359-61.
- [35] Röschke J, Wagner P, Mann K, Prentice-Cuntz T, Frank C. An analysis of the brain's transfer properties in schizophrenia: Amplitude frequency characteristics and evoked potentials during sleep. *Biol Psychiatry.* 1998;43(7):503-10.
- [36] Sarkar S, Katsush MZ, Nizamie SH, Prharaj SK. Slow wave sleep deficits as a trait marker in patients with schizophrenia. *Schizophr Res.* 2010;124(1-3):127-33.
- [37] Poulin J, Daoust AM, Forest G, Stip E, Godbout R. Sleep architecture and its clinical correlates in first episode and neuroleptic-naive patients with schizophrenia. *Schizophr Res.* 2003;62(1-2):147-53.

- [38] Castelnovo A, Casetta C, Donati F, Giudice RD, Zangani C, Sarasso S, et al. Sleep endophenotypes of schizophrenia: A high-density EEG study in drug-naïve, first episode psychosis patients. *Schizophrenia Bulletin*. 2020;46(Suppl 1):S32.
- [39] Oh SM, Lee YJ, Kim JW, Choi JW, Jeong DU. Preliminary study on quantitative sleep EEG characteristics in patients with schizophrenia. *Psychiatry Investig*. 2017;14(2):219-25.
- [40] Sekimoto M, Kato M, Watanabe T, Kajimura N, Takahashi K. Cortical regional differences of delta waves during all-night sleep in schizophrenia. *Schizophr Res*. 2011;126(1-3):284-90.
- [41] Forest G, Poulin J, Daoust AM, Lussier I, Stip E, Godbout R. Attention and non-REM sleep in neuroleptic-naïve persons with schizophrenia and control participants. *Psychiatry Res*. 2007;149(1-3):33-40.
- [42] Benson KL, Sullivan EV, Lim KO, Lauriello J, Zarcone VP Jr, Pfefferbaum A. Slow wave sleep and computed tomographic measures of brain morphology in schizophrenia. *Psychiatry Res*. 1996;60(2-3):125-34.

**PARTICULARS OF CONTRIBUTORS:**

1. Psychiatrist, Department of Psychiatry, Institute of Psychiatry-Centre of Excellence, IPGME&R, Kolkata, West Bengal, India.
2. Assistant Professor, Department of Psychiatry, Institute of Psychiatry-Centre of Excellence, IPGME&R, Kolkata, West Bengal, India.
3. Professor and Head, Department of Psychiatry, Institute of Psychiatry-Centre of Excellence, IPGME&R, Kolkata, West Bengal, India.
4. Assistant Professor, Department of Anatomy, AIIMS Kalyani, Kalyani, West Bengal, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Amit Kumar Pal,  
Assistant Professor, Department of Anatomy, AIIMS Kalyani, NH34 Connector,  
Basantapur, Saguna, Kalyani, Nadia-741245, West Bengal, India.  
E-mail: amit.anat@aiimskalyani.edu.in

**PLAGIARISM CHECKING METHODS:** [\[Jain H et al.\]](#)

- Plagiarism X-checker: Sep 21, 2023
- Manual Googling: Oct 19, 2023
- iThenticate Software: Nov 03, 2023 (14%)

**ETYMOLOGY:** Author Origin**EMENDATIONS:** 6**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Sep 21, 2023**Date of Peer Review: **Oct 13, 2023**Date of Acceptance: **Nov 06, 2023**Date of Publishing: **Dec 01, 2023**