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Original article

Sleep quality and cognitive impairments in remitted patients with schizophrenia in Nigeria

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ABSTRACT

Background. – Despite the ubiquity of sleep disturbance in schizophrenia, it has generally been overlooked as a potential contributor to cognitive impairments. The main aim of this study was to find out if impaired sleep quality contributes to cognitive impairments in patients with a diagnosis of schizophrenia who are in remission.
Methods. – The study was conducted at the University College Hospital, Ibadan and State Hospital, Ibadan, Nigeria. The Pittsburgh Sleep Quality Index (PSQI) and Screen for Cognitive Impairment in Psychiatry (SCIP) were applied in this cross-sectional study, to all consecutive and consenting remitted outpatients with schizophrenia ($N = 130$). Other instruments such as Hamilton Depression Rating Scale (HDRS), the Positive and Negative Syndrome Scale (PANSS), sociodemographic and clinical measures were also applied.
Results. – There were 130 participants made up of 69 females (53.1%) and 61males(46.9%). The mean age of the participants was 38.5 ± 9.1 years. The prevalence of poor sleep quality in remitted patients with schizophrenia was 56.9%. Sleep quality was significantly negatively correlated with Verbal Learning Test-Immediate (VLT-I) ($r(128) = -.18$, $P = .044$) and Verbal Learning Test-Delayed (VLT-D) ($r(128) = -.18$, $P = .037$). The variables that independently predicted cognitive functioning were the VLT-I, odds ratio (OR) 0.66; 95% confidence interval ((CI) 0.49-0.88) and education (OR) 0.61;(CI) 0.40- 0.92).
Conclusion. – Poor subjective sleep quality measured by the PSQI is linked to cognitive impairment in remitted patients with schizophrenia. We suggest that sleep quality in remitted patients with a diagnosis of schizophrenia should receive better attention by physicians.

1. Background

There is increasing recognition of the importance of sleep quality in patients with schizophrenia [1,2]. Sleep disturbance has been consistently reported in patients with schizophrenia, independent of the phase of the illness [3,4]. Contrary to certain misconceptions, many patients with schizophrenia have enduring symptoms including sleep disturbance, despite being in remission. The sleep problems include early morning awakening, difficulties with falling asleep, being unable to go back to sleep, an inclination for being awake at night, decreased deep or slow-wave sleep and short REM latencies [5–7]. These sleep problems are underestimated in many patients with schizophrenia [8]. Between 30% to 80% of patients with schizophrenia experience sleep problems [4]. The quality of sleep is a predictor of impaired functioning in people with a diagnosis of schizophrenia [9]. Conversely, treating insomnia has been shown to lower the severity of psychotic symptoms in patients with schizophrenia [10]. Unfortunately, because sleep disorders are difficult to separate from the primary diagnosis of schizophrenia, very few studies have examined sleep quality in patients with a diagnosis of schizophrenia [1,11]. Most of the studies on sleep disturbance in schizophrenia have focused on insomnia [12,13]. Additionally, sleep disorders are often not the principal focus of clinicians treating patients with schizophrenia. Abnormalities in sleep quality and cognitive impairments are common in patients with a diagnosis of schizophrenia. There is the notion that the two domains (sleep quality and cognitive impairment) may be linked. More precisely, impaired sleep quality may give rise to cognitive impairments in patients with schizophrenia [2,4]. Unfortunately, there have been varying reports on this association. The variations have been compounded by studying patients at different phases of the schizophrenic illness. For example, while Zavecz et al. showed

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that there is no association between subjective sleep quality and cognitive performance in the domains of working memory [14], Van den Noort et al. (2016) indicated that a negative relationship exists between sleep quality and working memory [8]. To date, not enough attention has been paid to the treatment of sleep problems in patients with schizophrenia. Certain sleep parameters such as sleep latency, sleep efficiency, Slow Wave Sleep (SWS), REM sleep have been shown to correlate with certain characteristics of schizophrenia such as the severity of illness, neurocognitive impairment and brain structure [4]. However, such associations have not been adequately quantified using standardized measures, especially in non-Caucasian populations. Using a standardized definition of remission i.e. the Remission in Schizophrenia Working Group Criteria [15], we sought to explore the correlates of sleep quality and neurocognitive impairments (NCI) in remitted patients with schizophrenia in Southwest Nigeria. The main aim of this study was to find out if impaired sleep quality contributes to cognitive impairments in patients with a diagnosis of schizophrenia.

2. Methods

The current investigation is part of a larger study titled, an exploration of the Multifaceted Dimensions of the Burden of Bipolar Disorders in Ibadan, South-West Nigeria (Mulberry Study) [16]. It was conducted at the Department of Psychiatry, University College Hospital, Ibadan Nigeria, and State Hospital, Adeoyo, Ibadan, Nigeria between 23 February and 10 October 2018, and was funded by Tertiary Education Trust Fund (TETFund) in Nigeria. The protocol and procedures were reviewed and approved by the Oyo State Research Ethical Review Committee (AD13/479/746). Participants provided written, informed consent before interviews and assessments were conducted.

2.1. Participants

The participants for the present study comprised patients with schizophrenia in remission. Remission was as defined by the Remission in Schizophrenia Working Group [15]. The diagnosis of schizophrenia was made according to criteria in the Diagnostic and Statistical Manual for Mental Disorders-Fourth edition (DSMIV) and validated using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)by the research assistants. Patients were eligible if they were aged between 18 and 60 years. All eligible patients were informed about the study, and the procedure was explained to them in Yoruba or English. The exclusion criteria were suffering from a severe medical or neurological condition or another psychiatric disorder that required treatment and inability to read or write. Remission was defined according to the Remission in Schizophrenia Working Group criteria for patients with a diagnosis of schizophrenia [15]. This definition required that the P1, P2, P3, N1, N4, N6, G5 and G9 items of the PANSS [17] must have a score of ≤ 3 points. Due to the cross-sectional nature of our research, clinical remission was assessed taking into account only the severity criterion (The 6-month duration criterion was not taken into consideration). Only 130 participants met the inclusion criteria for remission according to the Remission in Schizophrenia Working Group criteria for patients with a diagnosis of schizophrenia. Consequently, only 130 participants were included in the current analysis.

2.2. Measures

2.2.1. The Pittsburgh sleep quality index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) [18] is a self-rated questionnaire which assesses sleep quality and disturbances over a-month time interval [19]. It distinguishes between "good sleepers" and "poor sleepers". It consists of 19 items covering seven components. The seven components are sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication and daytime dysfunction. Individual scores range in each of the seven components from 0 to 3 with "0" indicating no difficulty and "3" indicating severe difficulty. The sum of the scores for these seven components yields one global score of 0 to 21. Higher scores indicate poorer sleep quality. A PSQI total score of >5 is indicative of poor sleep [19] and distinguishes good and poor sleepers [19]. This score (i.e. >5) yields a diagnostic sensitivity of 89.6% and specificity of 86.5%. The PSQI has good internal consistency and test-retest reliability.

2.2.2. Screen for Cognitive Impairment in Psychiatry (SCIP)

The SCIP is a brief screening tool designed to detect cognitive impairment in psychiatric patients with psychotic or affective disorders [20]. Three alternative forms of the scale are available to aid repeated testing while reducing learning effects. It has five subtests:

- Verbal Learning Test-Immediate (VLT-I) for assessing immediate verbal learning;
- Verbal Learning Test-Delayed (VLT-D) for assessing delayed verbal learning;
- Working Memory Test (WMT) for assessing working memory;
- Verbal Fluency Test (VFT) for verbal fluency;
- Processing Speed Test (PST) for assessing processing speed.

The original version of the SCIP is in English [20]. The SCIP shows adequate psychometric properties for the detection of cognitive impairment in patients with psychotic disorders e.g. schizophrenia and affective disorders e.g. bipolar affective disorder [21,22].

The criteria to differentiate between the cognitively impaired and non-cognitively impaired participants was based on SCIP scores derived from 100 healthy controls recruited during the study [19]. We transformed total scores into z scores using the means and standard deviations obtained from controls recruited during the study. The Z-score was calculated by subtracting the group mean from a patient's score, divided by the standard deviation. Then we dichotomized the z scores for the global index score. Z scores under -1 were considered as cognitively impaired [23,24].

2.2.3. Hamilton Depression Rating Scale (HDRS)

It was used to measure the severity of depressive symptoms [25].

2.2.4. The Positive and Negative Syndrome Scale (PANSS)

The PANSS was used for assessing positive, negative, and general psychopathology associated with schizophrenia [17].

2.2.5. The Structured Clinical Interview for DSM-IV (SCID-I/P)

It is a semi-structured interview that guides the user step-by-step through the DSM-IV diagnostic process [26].

2.2.6. Other measures

Other measures such as sociodemographic and clinical information were obtained from all patients. These included age, age at onset of the first episode, gender, years of education, antipsychotic dose and type, work status, marital status and medical comorbidity. Antipsychotics taken by participants were converted into haloperidol equivalent doses.

3. Results

3.1. Sociodemographic and clinical characteristics of participants

There were 130 participants made up of 69 females (53.1%) and 61males (46.9%). The mean age of the participants was 38.5 ± 9.1

Table 1
Sociodemographic and clinical characteristics of participants.

Characteristic	Mean (S.D)
Age (years)	38.5(9.1)
Age at onset of first episode (years)	29.0(7.9)
Education (years)	13.4(3.3)
Antipsychotic dose (mg/day) (haloperidol equivalents)	3.6(5.7) Range = 0-55.0; Mdn[c] = 2.0
Pittsburgh Sleep Questionnaire Index (PSQI) Global score	5.3(3.1)
HDRS[a] total score	4.78(4.58)
PANSS[b] (positive subscale)	8.55(2.36)
PANSS (negative subscale)	10.5(3.3)
PANSS (general subscale)	20.6(3.9)
PANSS (total score)	39.6(7.2)
Gender *N*(%)	
Male	61(46.9)
Female	69(53.1)
Work status	
Employed *N*(%)	88(67.7)
Unemployed *N* (%)	42(32.3)
Marital status *N*(%)	
Single/Never married *N*(%)	61(46.9)
Married/Cohabiting *N* (%)	45(34.6)
Divorced/Widowed/Separated *N* (%)	24(18.5)
Medical comorbidity	
Absent *N*(%)	125(96.2)
Present *N*(%)	5(3.8)
Antipsychotics type	
Atypical only *N*(%)	42(32.3)
Atypical +Typical *N*(%)	23(17.7)
Typical only *N*(%)	60(46.2)

Z = Data are presented as mean ± SD unless otherwise indicated. Percentages may not sum up to 100 because of missing data
[a] Hamilton Rating Scale for Depression.
[b] Positive and Negative Syndrome Scale.
[c] Median.

Table 2
Correlations between cognitive impairment and sleep quality.

	r	*P*-value
VLT-I	−.177	0.044
WMT	−0.066	0.455
VFT	−0.098	0.268
VLT-D	−.183	0.037
PST	−0.075	0.393
SCIP total score.	−0.158	0.073

VLT-I: Verbal Learning Test-Immediate; WMT: Working Memory Test; VFT: Verbal Fluency Test; VLT-D: Verbal Learning Test- Delayed; PST: Processing Speed Test; Total SCIP: SCIP total score.

Table 3
Independent predictors of cognitive impairment.

Characteristics	OR	95% C.I. for OR		*P*-value
		Lower	Upper	
Sleep quality				
Poor sleepers	1.000			
Good sleepers	0.529	0.189	1.481	0.225
PANSS positive subscale	1.199	0.974	1.476	0.087
Antipsychotic type				
Typical antipsychotic	1.000			
Atypical antipsychotic	0.476	0.147	1.540	0.215
Atypical + typical antipsychotic	1.984	0.533	7.388	0.307
VLT-I	0.762	0.633	0.916	0.004
VLT-D	0.781	0.590	1.034	0.085
Education (years)	0.662	0.525	0.835	0.001
Excessive sleepiness				
Present	1.000			
Absent	1.609	0.135	19.162	0.707
Sleep duration				
Inadequate	1.000			
Adequate	3.837	0.410	35.945	0.239

VLT-I: Verbal Learning Test-Immediate; VLT-D: Verbal Learning Test- Delayed. PANSS: Positive and Negative Syndrome Scale. OR: Odds Ratio.

years. Most (67.7%) of the participants were employed. The mean psychopathology score on the PANSS was 39.9 ± 7.2 while the mean depression score on the HDRS was 4.78 ± 4.58 (Table 1).

3.2. Prevalence of poor sleep quality in remitted patients with schizophrenia

The prevalence of poor sleep quality in remitted patients with schizophrenia was 56.9%. There was no significant difference in the proportion of poor sleepers between male and female participants X^2=.374 (1) *P*=.541.

3.3. Cognitive function and characteristics of the participants

The participants with cognitive impairment were similar to the participants without cognitive impairment except the proportion of patients on typical/atypical antipsychotics, education and severity of psychopathology on the positive subscale of the PANSS ($P < 0.05$).

3.4. Correlation

Table 2 shows the correlations of each subtest of the SCIP with the sleep quality (global PSQI) in the participants. VLT-I = Verbal Learning Test-Immediate and VLT-D = Verbal Learning Test-Delayed were significantly negatively correlated with sleep quality.

3.5. Multivariate analysis

In the multivariate analysis, after including the variables that were significant at the bivariate level (< 0.05), as well as some variables that can affect cognitive functioning (duration of sleep andsleepiness), the variables that independently predicted cognitive functioning were the education and the VLT-I* = Verbal Learning Test-Immediate (Table 3).

4. Discussion

The main aim of the present study was to investigate if impaired sleep quality contributes to cognitive impairments in patients with a diagnosis of schizophrenia, who are in remission. The main findings were that declarative memory (both immediate (VLT-I) and delayed (VLT-D)) were significantly negatively correlated with sleep quality in this patient group. More precisely, we found that Verbal Learning Test-Immediate and education predicted cognitive functioning. The finding that sleep quality is associated with cognitive impairment is in keeping with existing studies [27–29]. The relationship between sleep and cognition in patients with a diagnosis of schizophrenia has been partly linked to the high levels of kynurenicin in the brain. Kynurenic acid is a neuroactive metabolite of kynurenine. Evidence suggests that abnormally high Kynurenic acid (an endogenous glutamate antagonist with action at the glycine-site of the N-methyl-D-aspartate-receptor) levels are involved in the pathophysiology of schizophrenia [30]. Elevated brain level of brain Kynurenic acid is associated with learning and memory. In adult male Wistar rats, higher levels of kynurenic acid were shown to be significantly associated with less rapid eye movement, REM sleep duration and suppressed theta power during REM sleep. REM sleep is the sleep phase in which dreams occur, and it is thought to be important for the consolidation of previous learning [31].

Contrary to our findings, Baandrup et al. (2017) indicated that cognitive impairment is not associated with sleep quality [32]. A plausible cause of this incongruity is that while our study captured the respondent's sleep experience and quality for the past month, the study by Baandrup et al. examined sleep spindle activity and morphology. Existing studies have found poor agreement between the self-reported and objective measurement of sleep disturbances [33].

Verbal Learning Test-Immediate and Delayed were significantly negatively correlated with sleep quality. Both VLT-I and VLT-D measure declarative memory. Memories undergo a process of system consolidation during sleep. Sleep disturbance in schizophrenia disrupts attention and impairs memory consolidation. It is thought that this sleep-dependent impairment contributes considerably to the cognitive deficits in schizophrenia [34].

Amongst the 130 patients with a diagnosis of schizophrenia who participated in the study, 56.9% were identified as having poor sleep quality (i.e. PSQI > 5). This estimate is higher than the prevalence of poor sleep quality reported in a similar study among patients with schizophrenia on treatment (i.e.45.4%) as reported by Ritsner, Kurs [35]. The prevalence of poor sleep quality (56.9%) found in the current study was also higher than rates previously reported in the general population (20- 30%) [36,37].

Our study has certain limitations. First, the assessment of sleep quality was subjective. Objective sleep assessments are often at variance with subjective sleep assessment. Additional studies assessing sleep objectively are needed to examine the sleep-related biological factors associated with cognitive function. Second, we employed a cross-sectional design, therefore, the causal relationships between sleep quality and cognitive function could not be explored. Third, the SCIP is a screening instrument and is somewhat limited in its ability to detect cognitive impairment. The use of a more elaborate cognitive assessment instrument such as the Brief Assessment of Cognition in Schizophrenia (BACS) could have yielded more robust associations than what we found. Also, the quality of sleep was only assessed on a declarative instrument, admittedly validated but it is very limited, especially since the only parameters retained for analysis are the overall score of the PSQI, the "good sleep" and that of "poor sleep" scores.

In conclusion, the results from the current study indicated that sleep disturbances are common in remitted patients with a diagnosis of schizophrenia. This should be actively treated like in other comorbid psychiatric disorders. We also showed that poor subjective sleep quality measured by the PSQI was linked to cognitive impairment. We suggest that sleep quality in remitted patients with a diagnosis of schizophrenia should receive better attention by physicians because poor sleep quality is related to cognitive impairment.

Compliance with ethical standards

All participants provided written informed consent. The study was conducted following the guidelines laid down in the Declaration of Helsinki. The protocol and procedures were reviewed and approved by the Oyo State Research Ethical Review Committee (AD13/479/746).

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Disclosure of interest

The authors declare that they have no competing interest.

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