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To cite this article: Cigdem Sahbaz & Ayse Kurtulmus (2019) Association between emotional functioning and biological rhythm disruptions in patients with schizophrenia, *Psychiatry and Clinical Psychopharmacology*, 29:4, 455-462, DOI: [10.1080/24750573.2019.1682853](https://doi.org/10.1080/24750573.2019.1682853)

To link to this article: <https://doi.org/10.1080/24750573.2019.1682853>



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Published online: 04 Nov 2019.



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# Association between emotional functioning and biological rhythm disruptions in patients with schizophrenia

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## ABSTRACT

**Objective:** Dysregulation of biological rhythm is associated with reduced executive functioning and potentiating psychosis, which are essential for the Theory of Mind (ToM) among patients with schizophrenia. However, the association between cognitive dysfunction, emotional information and disruption of biological rhythm remains uncertain.

**Methods:** Forty-one patients with schizophrenia and forty age, gender and smoking status-matched healthy controls were recruited into the study. The Wisconsin Card Sorting Test (WCST), The Stroop test, The Reading the Mind in the Eyes Test (RMET), The Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) were used.

**Results:** BRIAN total, sleep, activity and social scores were higher in patients with schizophrenia than healthy controls. Higher BRIAN score was correlated with lower RMET score; with higher PANSS total, positive and negative scores, and not correlated with executive functions. In the regression analysis, it was observed that gender and increased BRIAN score was independently associated with lower scores for RMET in a patient with schizophrenia.

**Conclusion:** These results suggest that the disruption of biological rhythm might be associated with ToM in patients with schizophrenia. Future research should examine the relationship between biological rhythm and ToM to determine if any causal associations can be identified.

## ARTICLE HISTORY

Received 30 August 2019  
Accepted 16 October 2019

## KEYWORDS

Schizophrenia; cognition;  
ToM; biological rhythm;  
BRIAN; social impairment

## Introduction



Cognitive dysfunction and emotional information deficits have mainly been reported in patients with schizophrenia, but their association with disruption of biological rhythm remains uncertain. Almost 50% of patients with schizophrenia showed markedly delayed and free-running sleep-wake cycles, and these sleep-wake shifts were always associated with the disrupted biological rhythm [1,2]. The disruption of biological rhythm often presents before the onset of schizophrenia and have been found associated with symptom exacerbation, including potentiating psychosis and cognitive impairments [3].

Regulation of sleep and cognitive functions have shared standard neuroanatomical and neurochemical bases, and the neuroimaging studies deduce that sleep deprivation negatively affects the prefrontal cortex, a neural system central to executive functions [4]. Also, disruption of sleep found associated with the altered connectivity in the fronto-striatal networks, and impaired fronto-striatal connections are associated with deficits of executive functions [5]. The glutamatergic and cholinergic transmission is critically involved both in cognition [6] and modulation of the sleep-wake cycle [3]. Genetic variability in biological clock genes, which play a central role in regulating biological

rhythms, have found to be associated with cognitive function following sleep loss [7]. These genes are also related to midbrain dopamine regulation and reward processing that known to be disrupted in patients with schizophrenia [8]. Besides the executive functions, increased magnitude of amygdala activity was found with a loss of functional connectivity with the medial prefrontal cortex, which area is also needed the key modulation for the proper function of affective ToM [9,10].

ToM expresses the essential emotional functioning and refers to the ability to attribute mental states to oneself and others [11] and refer to the psychological needs of a person to be a part of a social group. Patients with schizophrenia have been documented the impairments of perceiving social cues since the prodromal phase of illness, and these social impairments have been found associated with severity of disease, compliance, clinical insight, insufficient functioning and outcome of treatment [12,13].

ToM is a core element of social functioning, and social input is one of the external environmental stimuli known as zeitgebers, which include light-dark cycles and locomotor activity that play a significant role in entraining the biological clock [14]. The impaired recognition of social inputs can be associated

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with misalignment of the biological rhythm and cause a decreased level of attendance daytime and functioning [15]. In a recent critical study, the authors proposed a model in which sleep loss promotes a self-reinforcing cycle of social functioning, and they suggested that the sleep loss causally can lead to a neuronal and behavioural phenotype of social impairments and loneliness in humans [16].

However, while in the current literature, some studies investigated the relationship between disruption of biological rhythm and executive cognitive functioning in patients with schizophrenia [17–20] no study have investigated the relationship between emotional functioning and biological rhythm in patients with schizophrenia. Therefore, our research aims to investigate the relationship between disruption of biological rhythm and executive functions to include ToM ability in patients with schizophrenia. Regarding the prior hypothesis, the patients with schizophrenia often present emotional dysfunction, social withdrawal, loneliness, and that might have a link with the biological rhythm disruptions. For exposing less to the daylight and social cues may cause impairment of social cognitive function; Thus, we expect to find a significant relationship between impairment of ToM/emotional functioning and disruption of biological rhythm in patients with schizophrenia than healthy controls.

Reading the mind in the eyes test (RMET) is used to assess the social cognitive ability of individuals. ToM ability has two distinct components: cognitive and affective. Two components of ToM can vary among ToM tasks, and impairments of the one component may not correspond to the other [4]. Therefore, in our study, we tried to understand the distinction between executive function and emotional functioning. Thus, we preferred to the RMET to assess the pure emotional component of ToM. Future research should examine the relationship between biological rhythm and ToM to determine if any causal associations would be determined to understand forming the basis of developing the emotional dysfunction in the patient with schizophrenia.

## Methods

### Participants

This study was performed in the outpatient psychiatry clinic of Bezmialem Vakif University. Forty-one patients with schizophrenia (SZ) and 40 healthy controls (HC) were recruited into the study between June 2017 to September 2017. The diagnosis was established through the Structured Clinical Interview for DSM-IV-TR, Clinical Version (SCID) [21]. The Positive and Negative Syndrome Scale (PANSS) was used to assess psychopathology. Patients with schizophrenia who had no acute psychotic episode, defined as PANSS general with a score <50 [22] in the past year were

recruited to the study. In total, 54 patients were eligible to participate with schizophrenia. Among those, 20 were referred from other psychiatry clinics; 34 had applied directly to our outpatient unit. In total, eight patients refused to participate to the study and five patients had an acute psychotic episode were excluded to the study. All subjects were between 18 and 65 years old. The patients with schizophrenia and HC were excluded from the study based on the following: unwillingness to participate, illiteracy, mental retardation, severe neurological and medical illnesses, alcohol or drug abuse or dependence (except for nicotine), history of head trauma, being shift worker.

## Measurements

### Clinical and sociodemographic measures

The sociodemographic form was used to collect information about age, gender, marital status, education, employment status, onset and course of the illness, ongoing psychotropic treatment and smoking status. Clinical symptomatology was assessed using the Positive and Negative Syndrome Scale (PANSS) [23].

The self-report Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) was used to assess biological rhythm disturbances [24]. The BRIAN questionnaire is retrospective for the last 15 days and includes 18 items split into four primary areas related to circadian rhythm disturbance: Sleep, Activity, Social rhythm, and Eating pattern. Each question is scored out of a possible four points, totalling an overall minimum score of 18 and a maximum score of 72. Higher scores indicate more significant biological rhythm disruption. Reliability and Validity of the Turkish version of Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) were conducted by Aydemir et al. [25].

### Neuropsychological measures

**Wisconsin card sorting test (WCST).** WCST was used to examine executive functions [26]. The computerized version of the Wisconsin card sorting test, developed by Wang Laboratories (version: WCST-CV4), was used, and performances were automatically scored by the computer. In the computer version of the WCST, the subject is presented with stimulus cards with various symbols on them. The cards differ in the colour, number, and the shape of the symbols. The subject is expected to find the matching rule according to verbal feedbacks given as “right” or “wrong.” During the test, the matching rules are changed, and the subject must notice the new rule to be successful. First, matching should be made according to the colour of the symbols. This rule changes after the subject correctly match ten cards with the colours. The subject is then expected to match the cards according to the shape of the symbols. This rule also changes after the subject correctly

matches ten cards with the shapes. Finally, matching is made according to the number of symbols on the cards. The dependent variables are the number of correct answers, number of categories completed and number of perseverative errors.

**Stroop test.** Stroop Test measures selective attention and processing speed, as well as executive function and cognitive flexibility [27]. The Stroop Test TBAG form was used in this study, which was based on the combination of the original Stroop Test and the Victoria Form [28]. It consists of 4 cards and five sections. The time difference between colour and word reading tasks (Section 2 and 5) provided the performance measures [29].

**Reading the mind in the eyes test (RMET).** RMET requires the identification of a word that best describes how a person is thinking or feeling based on photographs presented to them of the eye regions of human faces and is dependent on emotional facial processing. The revised version of the Eyes Test is an advanced Theory of Mind (ToM) task, which contains 36 black and white photographs of the eye region [30]. Half of the photos depict females, and half depict males, and all involve complex cognitive and emotional states. Participants view the photos and are asked to choose the most accurate descriptor for the emotion that is portrayed. Four possible choices are provided with each photo. If the participants have any problem comprehending the meaning of each descriptor, a check sheet with definitions, and an example for each descriptor, is provided. Scoring consists of tallying the number of correct responses. The Turkish version of the test consists of 32 items and the validity and reliability studies made by Yildirim et al. [31].

The study was carried out by ethical principles for medical research involving humans (WMA, Declaration of Helsinki) and approved by the Ethics Committee of the Bezmialem University Medical Faculty in June 2017. All participants provided informed written consent for the study.

### Statistical analyses

The characteristics of the study sample and the comparison of raw cognitive test scores were reported using descriptive analyses. Student's *t*-test was used to compare normally distributed, and Mann-Whitney U- test for non-normally distributed continuous variables. For categorical variables, the differences among the groups were analyzed with the Chi-Square Test. One-way analysis of covariance (ANCOVA) was conducted to compare BRIAN total scores between groups after adjusting for age and gender. We also generated Z-score (individual score minus mean test score divided by the standard deviation) for each subscale

of neurocognitive tests. Then we calculated the compound score for executive function. Z-scores of Stroop-time difference, WCST- perseverative errors and WCST-categories were averaged to calculate the compound score for executive function. Compound executive function and ToM scores were compared in SZ and HC groups using ANCOVA adjusted for age and education level. Spearman's or Pearson's correlation tests were used to investigate the correlation of BRIAN total scores with cognitive domains and clinical symptoms in patients. Multiple linear regression analyses were applied with ToM scores as the dependent variable to investigate whether BRIAN total scores independently predict overall change on ToM abilities after the effects of other possible predictors (age, gender, PANSS total score) are considered. All analyses were conducted using SPSS version 20 (SPSS Inc., Chicago, IL). All tests of significance were two-tailed.

## Results

### Sociodemographic, clinical characteristics and cognitive test scores of SZ and HC

The clinical and sociodemographic characteristics of the subjects are presented in Table 1. The groups were not significantly different for age, gender and smoking status ( $p = .34$ ;  $p = .15$  and  $p = .43$ , respectively). The education level of HC was higher than patients ( $p = .004$ ), and the percentages of married and employed people were also higher in HC ( $p < .001$  and  $p < .001$ , respectively). Cognitive test profile of groups is also illustrated in Table 1. There were significant differences among the groups in all individual cognition scores. Additionally, the compound score (Z-scores) for executive functions was calculated to avoid false positive results of multiple testing. The compound executive function score was also significantly lower in the SZ group, after controlling for age and education level ( $p = .004$ ).

### Biological rhythm disturbances in patients with SZ

Patients with SZ showed significantly more significant biological rhythm disruptions than HCs. In comparison to the HC group, BRIAN total scores were significantly ( $42.67 \pm 10.79$  vs  $33.42 \pm 9.84$ ,  $F_{1,14} = 16.28$ ,  $p < .001$ ) and after adjusting for age and gender, the difference between groups remained significantly ( $F = 16.28$ ,  $\eta^2 = .18$ ,  $p < .001$ ) higher in the patients with SZ than in HC. Patients also had significantly higher alterations in sleep, activity and social rhythm subscales of BRIAN ( $F = 3.54$ ,  $p = .02$ ;  $Z = -3.69$ ,  $p < .001$  and  $Z = -3.87$ ,  $p < .001$ , respectively). There was no significant difference between study groups in terms of eating subscale score ( $Z = -0.87$ ,  $p = .39$ ) (Figure 1).

**Table 1.** Sociodemographic, clinical characteristics and cognitive test scores of studied population.

	SZ (n:41)	HC (n:40)	Test Statistics	p
Age (mean $\pm$ SD)	40.44 $\pm$ 10.81	42.83 $\pm$ 11.51	$t = -.96$	.34
Gender (female %)	% 39 (16/41)	% 55 (22/40)	$\chi^2 = 2.08$	.15
Marital status (married %)	% 14.6 (6/41)	% 65.0 (26/40)	$\chi^2 = 21.49$	<.001*
Education (years, mean $\pm$ SD)	7.34 $\pm$ 5.58	10.20 $\pm$ 4.86	$t = -3.00$	.004*
Employment status (unemployment %)	% 82.9 (34/41)	% 35.0 (14/40)	$\chi^2 = 19.26$	<.001*
Smoking (yes %)	% 51.2 (21/45)	% 42.5 (17/40)	$\chi^2 = .62$	.43
ToM (RMET Score)	15.42 $\pm$ 4.92	20.28 $\pm$ 4.45	$F = 16.01^a$	<.001*
Executive Functions				
WCST- perseverative errors	41.58 $\pm$ 20.60 (43.50)	35.19 $\pm$ 25.77 (32.35)	$Z = -2.33$	.03*
WCST- categories	1.92 $\pm$ 1.44 (32.33)	3.70 $\pm$ 2.94(43.82)	$Z = -2.22$	.02*
Stroop Time difference	27.01 $\pm$ 15.51 (50.35)	15.48 $\pm$ 8.59 (29.38)	$Z = -4.06$	<.001*
Compound score <sup>b</sup>	-0.34 $\pm$ 0.59	0.26 $\pm$ 0.85	$F = 9.08^a$	.004*
Duration of illness (mean $\pm$ SD)	16.39 $\pm$ 8.01			
Age of onset (mean $\pm$ SD)	24.24 $\pm$ 8.39			
CPZe (mg)	752.68 $\pm$ 474.38			
PANSS-Total (mean $\pm$ SD)	66.29 $\pm$ 14.30			
PANSS- Positive (mean $\pm$ SD)	14.71 $\pm$ 5.21			
PANSS- Negative (mean $\pm$ SD)	18.73 $\pm$ 6.38			
PANSS-General (mean $\pm$ SD)	32.85 $\pm$ 7.16			

SZ, Schizophrenia patients; HC, Healthy controls; ToM, Theory of Mind; RMET, Reading the Mind in the Eyes Test; WCST, Wisconsin Card Sorting Test; CPZe, Chlorpromazine equivalent dose; PANSS, Positive and Negative Syndrome Scale.

t: Student's *t*-test;  $\chi^2$ : chi-square test; Z: Mann-Whitney U test.

<sup>a</sup>One-way analysis of covariance (ANCOVA) adjusted for age and education level.

<sup>b</sup>Calculated by averaging the Z-scores of Stroop-time difference, WCST-categories and WCST-perseverative errors.

\* $p < .05$ .

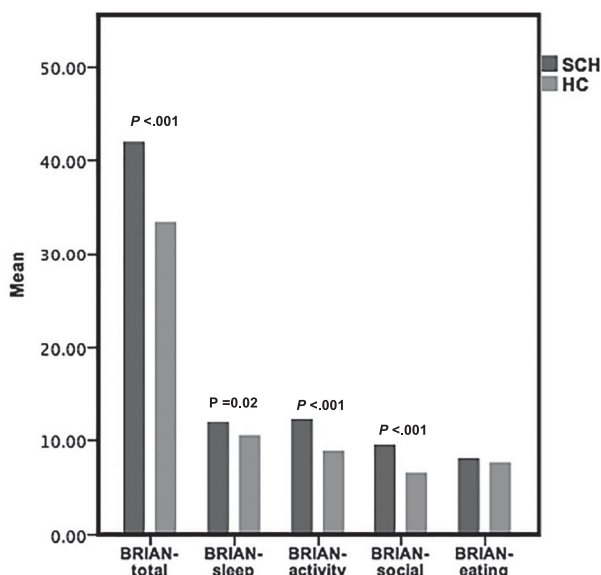
### Correlations between cognitive functions, symptom severity and biological rhythm disturbances

In patients, BRIAN total score was significantly negatively correlated with RMET scores ( $p = .02$ ). There was also a significant positive correlation between

BRIAN total score and PANSS total and subscale scores ( $p = .002$ ;  $p = .04$ ,  $p < .001$  and  $p < .001$  for positive, negative, total and general PANSS scores, respectively) (Table 2). There was no significant correlation between BRIAN total score and executive functions ( $p = .60$ ). In patients, CPZe was significantly correlated with BRIAN total ( $p = 0.04$ ;  $r = 0.33$ ) and there was no correlation between BRIAN subscales ( $p = 0.25$ ,  $p = 0.12$ ,  $p = 0.08$ ,  $p = 0.07$  for sleep, activity, social and eating score, respectively); RMET ( $p = .50$ ) and executive functions ( $p = .27$ ).

### Multiple linear regression analysis on ToM scores

RMET score were regressed on age, gender, PANSS total score and disturbances of biological rhythm (BRIAN-total score) in patients. It was observed that gender and increased BRIAN total score was independently associated with lower score for RMET in the patients with SZ (Table 3). In HC, the same regression



**Figure 1.** Comparison of BRIAN total and subscale scores between patients and healthy controls. BRIAN total score and sleep, activity and social rhythm subscale scores were significantly higher in patient group than controls ( $p < .001$ ;  $p = .02$ ;  $p < .001$  and  $p < .001$ , respectively). There was no significant difference between study groups in terms of eating subscale score ( $p = .39$ ). Student's *t*-test was used to compare Brain total score and sleep subscale score; Mann-Whitney U test was used to compare activity, social rhythm and eating subscale scores. BRIAN: Biological Rhythm Interview of Assessment in Neuropsychiatry.

**Table 2.** The correlation of BRIAN total scores with cognitive domains and clinical symptoms in patient group.

	Test Statistics	p
ToM (RMET Score)	$\rho = -.38$	.02*
Executive Functions <sup>a</sup>	$\rho = -.09$	.60
PANSS-total	$\rho = .60$	<.001*
PANSS-positive	$r = .48$	.002*
PANSS-negative	$r = .33$	.04*
PANSS-general	$\rho = 0.67$	<.001*

BRIAN, Biological Rhythms Interview of Assessment in Neuropsychiatry; ToM, Theory of Mind; RMET, Reading the Mind in the Eyes Test; PANSS, Positive and Negative Syndrome Scale.

$\rho$  = Pearson correlation coefficient,  $r$  = Spearman's rank correlation coefficient.

<sup>a</sup>Calculated by averaging the Z-scores of Stroop-time difference, WCST-categories and WCST-perseverative errors.

\* $p < .05$ .



**Table 3.** Regression analysis on ToM scores in patient group.

	<i>B</i>	<i>SE</i>	$\beta$	<i>t</i>	<i>p</i>
Age	-.11	.07	-.24	-1.68	.10
Gender <sup>a</sup>	3.53	1.41	.35	2.50	<b>.02*</b>
PANSS-total score	-.002	.06	-.006	-.04	.97
BRIAN	-.179	.08	-.39	-2.27	<b>.03*</b>

ToM, Theory of Mind; PANSS, Positive and Negative Syndrome Scale; BRIAN, Biological Rhythms Interview of Assessment in Neuropsychiatry.

*B* = Unstandardized beta coefficient; *SE* = Standard error;  $\beta$  = Standardized beta coefficient.

<sup>a</sup>Gender: 1 = Male; 0 = Female

\**p* < .05.

analysis revealed that age was the only predictor for ToM scores ( $B = -.14$ ,  $SE = 3.74$ ,  $\beta = -.36$ ,  $t = -2.33$ ,  $p = .03$ ), whereas gender and BRIAN total score were not significantly correlated with RMET score.

## Discussion

To our knowledge, this is the first study to investigate the relationship between the executive and emotional functioning in addition to subjective measures of biological rhythm in patients with schizophrenia. The significant finding of this study was the patients with schizophrenia showed significantly higher disruptions of biological rhythm than healthy controls and that disruptions were associated with lower performance on emotional functioning (ToM ability). Furthermore, increased levels of disruption of biological rhythm (BRIAN score) and gender predict strongly facial recognition (RMET score) nor then other variables in patients with schizophrenia.

Some evidence suggested that poor and inadequate sleep may be associated with ToM impairments due to brain regions involved in the sleep-wake homeostasis, and the biological rhythm also seems to correspond to both emotional information processes and ToM deficits [4]. The amygdala and fusiform gyrus implicated in the performance of the affective facial recognition and emotional information processing/regulation [4]. Sleep-deprivation (SD) can activate amygdala with greater magnitude, and this demonstrates that shortened sleep duration intensifies emotional reactivity, and it causes reduced functional connectivity between the amygdala and medial prefrontal cortex (an area found to be responsible in the feedback of emotional processing) [10].

Shorter sleep and quality of sleep has also been associated with emotional information in both adults and youth and suggested with studies that they predict poor performance to identify pure facial emotions [4,32] and to match emotions to faces [33]. The recent analysis demonstrated the role of negative affect in the relationship between sleep problems and paranoia [34]. The data on the interplay between insomnia and emotion proposes that insomnia can provide to strengthen the effect of negative experiences [35]. For

example, one study found that reduced sleep not only exaggerated the negative emotional consequences of disturbed daytime experiences but also weakened the positive consequences of rewarding activities [36]. However, psychosis spectrum disorders are linked with a range of sleep problems and these findings based on the general population. Therefore, generalizing these data to clinical groups may be inaccurate, so caution must be taken [34].

Furthermore, our results showed that patients with schizophrenia had higher disruption of the biological rhythm (BRIAN-total score) than healthy controls. This finding fits well with previous findings that abnormalities of sleep and biological rhythm are often observed in patients with schizophrenia. The increased level of disruption on biological rhythm in schizophrenia has been supported, which showed that patients have higher circadian variation in sleep onset and sleep termination when compared to age-matched healthy controls [2]. Recent study identified the diurnal rhythms of the gene expression in the human dorsolateral prefrontal cortex and found that most of these transcripts are not rhythmic in subjects with schizophrenia compared than healthy controls [37]. Also, morning chronotype was found negatively correlated with schizophrenia and several of the mapped genes at the chronotype-associated loci are well-known schizophrenia loci and suggested that a shared biological mechanism between chronotype and schizophrenia risk [38]. Furthermore, duration of illness, age, type, or dosage of antipsychotic medication have not found related to biological rhythm disruption in patients with schizophrenia [2,17].

The patients with schizophrenia also displayed worse disruption in the BRIAN social and activity subdomains addition to the total score and sleep domain. The impaired social skill can be associated with circadian misalignment and misaligned biological rhythm cause the decreased level of attendance daytime and functioning [15]. For instance, physical activity has been found significantly lower in non-medicated patients with schizophrenia and identify with reduced cognitive function and the increased level of severity of illness. As mentioned previously, the locomotor activity can reset as an entraining signal and represent a mechanism for endogenous behaviour to feedback and change following circadian functions. Therefore, in the same study, the authors suggested that the exercise or optimize daily activity might be as a non-pharmacological treatment option in psychosis for improving social adjustment or quality of life in patients with schizophrenia [15].

In our sample, there was also a significant positive correlation between BRIAN scores and positive, negative, and total PANSS scores. Our findings are in line with the literature, which is suggested that sleep and circadian misalignment might be associated with the

severity of schizophrenia. The relationship between shorter sleep duration and delusional ideas and hallucinations have been reported [39] and also found to be highly predictive of transition to psychotic episode in the following 18 month period in adolescents and young adults at high risk [40]. Sleep disturbances often accompany schizophrenia and maybe another pathophysiological component of the disorder. Most of the patients with schizophrenia experience sleep problems such as difficulties in sleep-onset and sleep-maintenance, reduced total sleep duration and sleep efficiency, and increased sleep latency, which is irrespective of the disease stage and clinical course of the disease [17]. It has been consistently shown that sleep deprivation in healthy individuals can cause psychotic-like features, including hallucinations, delusions, cognitive impairments, and mood alterations, which strongly resemble the core features of schizophrenia [3,41]. Thus, sleep deprivation has been considered as a model of psychosis in laboratory settings. Not only in healthy individuals but also patients with schizophrenia have been found associated disruption in sleep with greater symptom severity and poor functioning in the next day [41].

We did not find a relationship between executive functions and domains of biological rhythm. We calculated the compound score (Z-scores) for executive functions to avoid false-positive results of multiple testing. The compound executive function score was also significantly lower in patients with schizophrenia after controlling for age and education level. There is evidence of associations between specific sleep and circadian parameters and performance in various cognitive tasks. For example, the daytime sleepiness, more fragmented sleep and delayed melatonin release was associated with the impairment of frontal lobe function tasks [17] and the circadian preferences, low secretion of melatonin, impairment of verbal memory (recognition) and Stroop task in patients with schizophrenia [19]. Also, spindle activity during stage 2 non-REM sleep in patients with schizophrenia has found associated with overnight improvements in functioning in a finger-tapping, sequence learning task [42]. Regarding the results, the possibility remains that the relationship between biological rhythm and cognitive performance might be task-specific, it would be appropriate to confirm the findings with the use of another cognitive batteries/task [19].

Regarding our literature search, no study was conducted with the BRIAN questionnaire in patients with schizophrenia. The BRIAN was developed with a focus on biological rhythm in patients with the mood disorder [24] and showed promising validity with the objective parameters of circadian rhythmicity, including actigraphy records [43] and level of urinary 6-sulfatoxymelatonin [44]. It also suggested

that and subjective measures (BRIAN) provide extensive evidence of sleep and biological rhythm system disruptions in mental disorders [44]. Also, the BRIAN appears to be a feasible tool to evaluate all domain of biological rhythms, due to the other scales that only indirectly measure biological rhythm by testing seasonality or chronotype or subjective quality of sleep [45].

We must note several limitations to our study. The cross-sectional nature of the study does not allow us to explore the causal relationships between biological rhythm disturbances and ToM. The BRIAN questionnaire measures retrospectively for the last 15 days of individuals. Also, the results cannot generalize for an extended period. Therefore, we included patients with no history of exacerbating psychosis within the last one year. We could not study with objective parameters in biological rhythms and sleep, and future investigations should both subjective and objective parameters of sleep, social, eating patterns in SZ. Also, using actigraphy should be considered for having high concordance with polysomnography in healthy adults and more extended recording periods (i.e. 7–14 days), which consider for a representative analysis of sleep and daily activity rhythm patterns. We included the patients in the study from a single outpatient clinic; a multi-centre study is required to test our results.

## Conclusion

The findings suggested that the disruption of biological rhythm might be strongly associated with ToM ability and severity of illness in patients with schizophrenia. While some studies have suggested misaligned biological rhythm with symptom exacerbation, including potentiating psychosis and cognitive impairments in schizophrenia, very few studies have investigated biological rhythm in patients with schizophrenia in great detail, including emotional functioning. The optimization of biological rhythm which might have a role to improve social impairments can be as a non-pharmacological treatment option in patients with schizophrenia. Further research with subjective and objective parameters and longitudinal investigations must be conducted to analyse causal relationships between biological rhythms and emotional functioning in patients with schizophrenia.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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