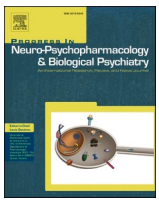
Progress in Neuropsychopharmacology & Biological Psychiatry 120 (2023) 110623

Contents lists available at ScienceDirect

Progress in Neuropsychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp



Circadian functioning and quality of life in substance use disorder patients with and without comorbid schizophrenia

Iman Hashemzadeh [a], José Francisco Navarro [b], Ana Adan [a,c,*]

[a] Department of Clinical Psychology and Psychobiology, School of Psychology, University of Barcelona, Passeig de la Vall d'Hebrón 171, Barcelona 08035, Spain
[b] Department of Psychobiology, School of Psychology, University of Málaga, Campus de Teatinos s/n, Málaga 29071, Spain
[c] Institute of Neurosciences, University of Barcelona, Barcelona 08035, Spain

ARTICLE INFO

Keywords:
Dual disorder
Substance use disorder
Schizophrenia
Sleep quality
Quality of life

ABSTRACT

Sleep disturbances are strongly linked with mental diseases such as substance use disorder (SUD) or schizophrenia (SZ) which can have a detrimental impact on quality of life (QOL), especially when both disorders are comorbid (dual disorder). In absence of studies about both circadian characteristics and QOL in patients with SUD and comorbid SZ (SUD + SZ), we examined a sample of 155 male under treatment, 75 with SUD + SZ and 80 only with SUD. Circadian functioning was evaluated by chronotype, social jet-lag and sleep quality (using the Pittsburgh Sleep Quality Index, PSQI), while the QOL was obtained by the World Health Organization's Quality of Life Questionnaire (WHOQOL)-BREF. SUD + SZ patients were more evening type than SUD, and this chronotype was linked to polydrug use in total sample and SUD + SZ group. We observed that the comorbidity did not lead to worse sleep quality in the SUD and SUD + SZ patients. QOL was poorer in SUD + SZ patients, who showed a negative association of Physical health, Psychological health and Social relationship with suicide attempts and severity of SZ. Lastly, patients with worse QOL also reported poorer sleep quality suggesting that treatment could include circadian adjustments along with a focused approach to lifestyle improvement.

1. Introduction

The most important functions of sleep are development and recovery of the brain functions (Galván, 2020), especially for having better mental and physical daily state. Sleep is part of one of the main circadian rhythms, the sleep-wake-cycle, resulting from the existence of an endogenous circadian clock. One of the most relevant and effective consequences of misalignment of the sleep-wake-cycle are sleep problems such as insomnia, difficulty in waking up in the morning, and drowsiness during the day, which are indicators that lead to request medication in sleep clinics (Bollu and Kaur, 2019).

The functioning of the human circadian clock implies an adjustment with the rhythmic environmental and social changes, being of special relevance the parameters of phase and regularity. The individual difference called chronotype is based on phase differences in circadian rhythms, which plays an important role in our daily habits. Individuals with chronotype categorized as morning-type prefer to wake up early in the morning, evening-type desire to fall asleep late and have difficulty waking up in the morning whereas intermediate or neither-type people tend to do their tasks between morning and evening type times (Adan et al., 2012). The consideration of the rhythmic regularity between days has given rise to the concept of Social Jet-Lag (SJL), that evaluates the discrepancy between the weekends and weekdays sleep timing (Roenneberg, 2012). It is assumed to exist SJL when there is a discrepancy of two hours or more, which can have a negative effect on quality of life (QOL) and life style (Chang and Jang, 2019).

Sleep problems are strongly linked with mental health diseases, especially with substance use disorder (SUD) (Adan, 2013; Chakravorty et al., 2018; Hashemzadeh et al., 2021; Vetrova et al., 2020; Wilkerson et al., 2021) or schizophrenia (SZ) (Afonso et al., 2014; Klingaman et al., 2015; Laskemoen et al., 2019; Wilson and Argyropoulos, 2012; Wulff et al., 2012), that even can impact on the detrimental QOL observed in these patients (Afonso et al., 2014; Hofstetter et al., 2005; Xiang et al., 2009). The association between substance use and sleep problems is reciprocal, but sleep problems may provide a pathway to substance use as a mode of self-medication, which can become a vicious cycle in which each of these factors are mutually enhanced (Bootzin and Stevens, 2005; Prat and Adan, 2011). In addition, there are studies that have reported

* Corresponding author at: Department of Clinical Psychology and Psychobiology, School of Psychology, University of Barcelona, Passeig de la Vall d'Hebrón 171, Barcelona 08035, Spain.
E-mail address: aadan@ub.edu (A. Adan).

https://doi.org/10.1016/j.pnpbp.2022.110623
Received 23 May 2022; Received in revised form 10 August 2022; Accepted 22 August 2022
Available online 25 August 2022

the association of chronotype and addiction; in fact, the evening type individuals consume more substances in both non-clinical (Prat and Adan, 2011; Taylor et al., 2020; Wittmann et al., 2010) and clinical populations (Adan, 2013; Kervran et al., 2015; Kivelä et al., 2018). SUD confers a substantial burden of disease globally, afflicting 71.2 million people in 2017 (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018) (Pan et al., 2020).

SZ is a severe mental disorder with a prevalence of about 1% in the general population. SZ can present positive symptoms, such as delusions, abnormal motor behavior, disorganized thoughts, and hallucinations, as well as negative symptoms such as flattened affect, social withdrawal, and lack of enthusiasm and interest, alogia (reduced speech productivity), and anhedonia (diminished capacity to experience pleasure) considering a period of one month or longer for diagnosis (American Psychiatric Association (APA), 2013). Although there are very few studies that have analyzed disruptions in circadian rhythms of SZ (Afonso et al., 2014; Klingaman et al., 2015) and SUD comorbid SZ patients (SUD + SZ) (Serrano-Serrano et al., 2021), results indicate that sleep problems such as insomnia co-occur frequently (Robertson et al., 2019; Sharma et al., 2016; Xiang et al., 2009). These sleep disturbances have been observed in association with the SZ severity (Korenic et al., 2020; Reeve et al., 2019) or even could be a risk factor for illegal and violence behaviors (Chen et al., 2021). In SZ patients greater sleep time irregularity was also associated with later dinner and caffeine consumption schedules, poorer sleep quality, greater social rhythm irregularity, and more severe positive symptoms (Chung et al., 2018). Therefore, it not surprising that sleep irregularities in SZ patients have significant negative effects on their performance and life habits (Brissos et al., 2013; Costa et al., 2018). Although sleep and circadian rhythms disturbances are infrequently considered for the treatment of SUD or SZ, when the therapeutic approach takes them into account, benefits are observed in patients both in their sleep quality (Costa et al., 2018; Waite et al., 2016; Wilson and Argyropoulos, 2012) and psychiatric symptoms (Capella et al., 2018; Pritchett et al., 2012).

The term of dual disorder refers to SUD when co-occurs with other primary mental disease in the same person (Adan and Torrens, 2021). SUD + SZ is highly common (Adan et al., 2017a) and the evidence, regardless of culture, points to male gender (Addington and Addington, 2007; Brunette et al., 2018; Serrano-Serrano et al., 2021; Talamo et al., 2006), family history (Adan et al., 2017a; Serrano-Serrano et al., 2021), younger age and earlier age of SUD and/or SZ onset (Addington and Addington, 2007; Chen et al., 2018; Donoghue et al., 2014; Huber et al., 2016; Serrano-Serrano et al., 2021) are important risk factors. Some studies stated that SUD + SZ patients showed more maladaptive coping strategies to treatment, as less use of social support (Marquez-Arrico et al., 2015), and poorer QOL compared to SUD ones (Aras et al., 2013; Benaiges et al., 2012; Daigre et al., 2017). The best treatment for dual disorder patients requires consideration of the specificities of the comorbid mental disorders, along with an integrated intervention (Daigre et al., 2017; Drake et al., 2020; Juel et al., 2017; Murthy and Chand, 2012).

Given that many of published works on sleep problem on SUD or SUD + SZ patients have focused on pharmacological treatments (Klingaman et al., 2015) this study aims to draw further attention to the components of circadian functioning. Thus, chronotype, social jet-lag and characteristics of sleep were assessed, along with the QOL of patients under treatment with diagnosis of SUD and SUD + SZ. As far as we know, this study is the first to be done with this approach, which in turn should be considered as a hopeful and worthy help for the comprehensive treatment from a personalized perspective of SUD patients with and without SZ. Our main hypothesis is that both SUD and SUD + SZ patients will show altered circadian functioning and worse QQL, being more marked in SUD + SZ, as well as that a better circadian rhythmicity will be related to a greater QQL.

2. Material and methods

2.1. Participants

Participants included 155 male patients, 80 with SUD and 75 with SUD + SZ, who were referred to a psychiatric and an addiction center in Shiraz, Iran. They were selected according to the 5th edition of {American Psychiatric Association, 2013 #25}Diagnostic and Statistical Manual of mental disorders (DSM-5; APA, 2013). Inclusion criteria were: 1) ages between 18 and 55 years, 2) male gender, 3) current SUD in remission with abstinence period from 1 to 9 months with lack of relapses before participation with dependence on several drugs (alcohol is missing because, in Iran, people do not often use it for the sake of culture and its illegality), 4) current diagnosis of SZ in SUD + SZ patients, 5) being under treatment and with clinically stable psychiatric symptomatology, and 6) fluent in Persian language and native of Iran. The exclusion criteria were: 1) having a current substance-induced psychiatric disorder or a psychiatric disorder due to a medical condition according to DSM-5 criteria, 2) being unable to complete our instruments, and 3) receiving electroconvulsive therapy within 12 months before their participation.

2.2. Procedure

Previous to acceptance for participate in the study the research conditions were explained individually and thoroughly to each patient by the clinical psychologist. Patients were assessed individually, taking two days of recordings with a 2-h session each day for every patient. The patients were divided into SUD and SUD + SZ groups, based on the diagnosis according to DSM-5 criteria. All patients were in treatment for their clinical condition (SUD and SUD + SZ), in which the treatment of both disorders was done simultaneously by the same team with integrated intervention. The integrated intervention includes a combination of motivational interviewing, contingency and case management, cognitive behavioral therapy, social skills training and relapse prevention. This study was approved by the ethics committee of the Research Committee of the University of Barcelona (IRB00003099) and authorization from the research center of Shiraz University of medical science was also obtained.

2.3. Measures

2.3.1. Structured interview and clinical symptomatology assessment

An experienced psychiatrist and two skilled clinical psychologists chose the patients, based on the Structured Clinical Interview (SCID-5-CV) of the DSM-5 (APA, 2013). Sociodemographic data (e.g., age, marital status, social class, education, economic status, and employment status) and clinical variables (e.g., diagnosis, age of SUD onset, type of drug use, abstinence time, daily use of medication, suicide attempts, presence of organic pathology, personal psychiatric history, labor, legal and family problems) were obtained individually and extracted then reviewed from the medical history of centers. In addition, as clinical symptomatology assessment SUD + SZ patients completed the Persian version of Positive and Negative Syndrome Scale (PANSS) to determine the presence of symptomatology and severity of their SZ disorder (Navid et al., 2009). It consists of three subscales: The Positive syndrome (7 items), Negative syndrome (7 items), and General Psychopathology (16 items) (in the Persian version, this subscale has been converted into the three other subscales; Disruption, Excitement and Depression-anxiety). Each of the 30 items is supplemented by a specific definition, as well as detailed anchoring points for each of the seven possible rating points for increasing levels of psychopathology: 1) absent, 2) minimal, 3) mild, 4) moderate, 5) moderately severe, 6) severe and 7) extreme. Internal reliability for PANSS and its dimensions in our study was adequate (Positive symptoms $\alpha = 0.707$; Negative symptoms $\alpha = 0.721$; Disruption $\alpha = 0.715$; Excitement $\alpha = 0.725$; Depression-anxiety $\alpha = 0.705$;

and Total PANSS α = 0.813).

2.3.2. Circadian functioning and quality of life assessments

We used the reduced Morningness–Eveningness Questionnaire (rMEQ), SJL questionnaire and the Pittsburgh Sleep Quality Index (PSQI) for assessment of circadian functioning. The rMEQ contains five items and cut of scores (range from 4 to 25) for the chronotypes are: 4–11, evening type, 12–17, intermediate type, and 18–25, morning type (Adan and Almirall, 1991; Rahafar et al., 2015a). The Cronbach's alpha coefficient was acceptable for the total rMEQ in our total sample (0.702). The SJL questionnaire asks for the time to go to bed and get up on work days and free days to calculate the difference between mid-sleep on workdays (MSW) and free days (MSF) (Wittmann et al., 2006). To assess the sleep quality the Persian version of PSQI was used; this questionnaire includes seven dimensions as follows: sleep quality, sleep latency, duration of sleep, efficiency of sleep, sleep disturbance, medication use, and daytime dysfunction in which each scale takes score from zero to three. Total score ranges from 0 to 21 and on each scale 0 indicates a normal status, 1 a mild problem, 2 a moderate problem, and 3 a severe problem (Moghaddam et al., 2012). The Cronbach's alpha coefficient is acceptable for the total PSQI (0.703) in the present study.

Furthermore, for evaluating the QOL we used the shorter version of WHOQOL as World Health Organization's Quality of Life Questionnaire (WHOQOL)-BREF with 26 items (Nedjat et al., 2008). Each item ranges from 1 to 5; higher scores indicated better QOL and consisted of four major domains with adequate Cronbach alpha coefficient: Physical health (0.709), Psychological health (0.773), Social relationships (0.746), and Environment health (0.726). The internal reliability for total WHOQOL-BREF was high (0.902). It should be mentioned that the WHOQOL-BREF includes two items that are related to the general health status and general QOL of the respondent (overall QOL), being its internal reliability in our sample of 0.704.

2.4. Data analysis

Group differences in demographic and clinical variables were explored with *t*-test or Mann-Whitney *U* test for continuous variables and the Chi-square test for categorical variables. If the quantitative data conformed to normal distribution, the t-test was used; otherwise, the nonparametric Mann-Whitney U test was used instead. We used univariate analyses of covariance (ANCOVA) for explore differences in the total scores of the rMEQ and PSQI scales, considering the clinical groups (SUD and SUD + SZ) as independent variable and age as a covariate, since it could be a confounding factor. Also, a second ANCOVA analysis was performed adding the age of SUD onset as the covariate. To study differences of chronotype in PSQI scales, the ANCOVA analyses were repeated adding the chronotype as independent factor. We used multivariate analyses of covariance (MANCOVA) for the SJL parameters and WHOQOL-BREF dimensions, with clinical group as an independent variable and age as a covariate. Besides, a second MANCOVA analysis was also performed adding the age of onset of SUD as covariates. Finally additional MANCOVA analyses were performed for WHOQOL-BREF dimensions, first adding as factor the chronotype, and second adding the levels of PSQI dimensions. In all cases, post-hoc analyses were Bonferroni corrected and partial Eta-square (η_p^2) was estimated to measure the effect size considering that a value of 0.01 was low, 0.04 moderate, and 0.1 high.

Bivariate correlation analyses were performed for explore the relationships of quantitative clinical variables with rMEQ, PSQI dimensions, and WHOQOL-BREF dimensions. The significantly related variables were entered into the subsequent multiple linear stepwise regression analysis. Using Person correlation, the relationship between the total scores of QOL and PSQI was assessed. All analyses were performed using the SPSS (Statistical Package for the Social Sciences version 26.0) software. The tests were two-tailed with the type I error set at 5%.

3. Results

3.1. Sociodemographic and clinical characteristics

A significant age difference between the two groups was observed, being SUD + SZ patients younger than SUD ($p = 0.018$). Considering the academic class, the chi-square test revealed a significant difference between both groups ($p = 0.001$), the SUD + SZ group presented a higher proportion of middle school degree and lower university studies in comparison with SUD ($p = 0.035$ and $p = 0.002$ respectively). There was not any significant difference in marital status, socioeconomic and employment status (see Table 1).

Regarding clinical variables (see Table 2), the SUD+ SZ group showed an early age of SUD onset ($p = 0.001$), more rate of social phobia ($p = 0.031$), previous General Anxiety Disorder ($p = 0.018$) and use of daily medication ($p < 0.001$), compared to SUD ones. In type of substance use SUD patients reported more consumption of opium in comparison with SUD + SZ group ($p = 0.040$). Groups did not differ in the concomitance of pathology, family, legal and labor problems, number of substance use, abstinent time and suicide attempts. According to the severity of SZ disorder (PANSS scale), the patients reported more negative symptoms followed by positive, disruption, depression-anxiety and excitement respectively. Moreover, most of them determined as mild SZ (36%) although others were in moderate (33.3%) and severe SZ (30.7%).

3.2. Circadian functioning: Chronotype, Social jet-lag, quality and components of sleep

Considering the chronotype, the chi-square test showed that there was a significant difference between the two groups ($\chi^2_2 = 16.813$, $p < 0.001$). SUD patients were more likely to be intermediate type in

Table 1
Sociodemographic variables for the SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) groups. Mean, standard deviation, percentage, and statistical contrast (*t*-test or Chi-Square test).

Sociodemographic data	SUD ($N = 80$)	SUD + SZ ($N = 75$)	Statistical contrast
Age	39.58 ± 10.24	35.63 ± 10.28	$t_{(153)}$=2.401*
Marital status			χ^2_3=5.453
Single	25%	41.3%	
Married	62.5%	50.7%	
Divorced	8.8%	4%	
Widow/Widower	3.8%	4%	
Socio economic status			χ^2_3=7.936
High	21.25%	17.3%	
Middle	41.25%	36%	
Middle low	20%	38.7%	
Low	17.5%	8%	
Academic class			χ^2_4=18.361**
Illiterate	13.8%	8%	
Primary studies	13.8%	24%	
Middle school	18.8%	38.7%	
High school	32.5%	25.3%	
University studies	21.25%	4%	
Employment status			χ^2_2=1.736
Active	61.25%	52%	
Inactive	28.8%	38.7%	
Retired	10%	9.3%	

* $p < 0.05$;
** $p < 0.01$.

Table 2
Clinical characteristics for the SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) groups. Mean, standard deviation, percentage and statistical contrast (t-test or Chi-Square test).

Clinical data	SUD (N = 80)	SUD + SZ (N = 75)	Statistical contrast
Age of SUD onset	35.68 ± 9.22	30.85 ± 8.40	$t_{(153)}$=3.403**
Concomitance organic pathology[a]			χ^2_5=2.931
Hypertension	3.8%	6.7%	χ^2_1=0.500
Hypothyroidism	2.5%	1.3%	χ^2_1=0.333
Hyperthyroidism	3.8%	6.7%	χ^2_1=0.500
Irritable bowel syndrome	1.3%	4%	χ^2_1=1.001
Migraine	2.5%	2.7%	χ^2_1=0.004
Other disorders (Hepatitis B/C, Obesity, HIV, diabetes, epilepsy, respiratory problems)	18.8%	15%	χ^2_1=0.615
Personal psychiatric history[a]			χ^2_6=12.928*
Social phobia	6.3%	17.3%	χ^2_1=4.665*
General anxiety disorder	3.8%	14.6%	χ^2_1=4.571*
Panic disorder	6.3%	8%	χ^2_1=0.091
Obsessive compulsive disorder	5%	8%	χ^2_1=0.400
Somatic disorders	5%	9.3%	χ^2_1=0.818
Other disorders (eating disorders, PTSD, personality disorders)	13.8%	17%	χ^2_1=0.167
Suicide attempts	0.24 ± 0.53	0.15 ± 0.39	$t_{(153)}$=1.200
Presence of problems			
Legal problems status	16.3%	12%	χ^2_1=0.574
Labor problem status	20%	28%	χ^2_1=1.363
Family problems	27.5%	28%	χ^2_1=0.005
Type of Substance[a]			
Nicotine	77.5%	77.3%	χ^2_1=0.040
Opium	60%	40%	χ^2_1=4.202*
Crystal	37%	32%	χ^2_1=0.667
Heroin	31.3%	34.7%	χ^2_1=0.205
Other (shireh, hashish, cannabis)	21.3%	30.7%	χ^2_1=0.901
Number of substance use	2.05 ± 0.84	2.08 ± 0.88	$t_{(153)}$= − 0.217
Polydrug use	37.5%	42.6%	χ^2_1=0.065
Daily use of psychiatric medication	28.57%	87.10%	χ^2_1=15.622***
Abstinent time (month)	7.47 ± 0.94	7.08 ± 1.57	t_{130}=1.750
PANSS score		76.36 ± 27.94	
Positive symptoms		17.64 ± 9.12	
Negative symptoms		19.88 ± 9.15	
Disruption		17.01 ± 9.88	
Excitement		9.92 ± 4.74	
Depression-anxiety		11.91 ± 6.55	

PTSD: Post-traumatic stress disorder; PANSS: Positive and negative syndrome scale;
[a] Percentages will not equal 100 as each patient may be in more than one category at the same time;
* $p < 0.05$;
** $p < 0.01$;
*** $p < 0.001$.

comparison with SUD + SZ groups ($p = 0.002$), while SUD + SZ patients were more likely to be evening type compared with SUD group ($p = 0.007$) (see Table 3). Moreover, no bivariate correlations among rMEQ and the clinical variables were observed.

The total score of rMEQ differs between the SUD (13.92 ± 3.96) and SUD + SZ (12.32 ± 4.23) groups in the ANCOVA analysis using age as a covariate ($F_{(1.152)}$= 6.738; $\eta^2_p = 0.042$; $p = 0.010$) and also by adding the age of SUD onset of the covariate ($F_{(1.151)}$= 5.269; $\eta^2_p = 0.034$; $p = 0.023$). Moreover, comparison of the group means with the Iranian normative data (15.05 ± 3.71) (Rahafar et al., 2015b) indicated that SUD and SUD + SZ groups presented lower scores, being more evident in the SUD + SZ group (t_{341}= 5.46, $p < 0.001$) than in the SUD group (t_{346}= 2.350, $p = 0.019$). In addition, regarding relationship of clinical variables provided a significant difference between chronotypes in polydrug users. Thus, in the SUD group Intermediate type polydrug users were more observable as compared with morning type and evening type ($p < 0.05$, in both cases), but evening type polydrug users were more than morning type ($p < 0.001$) and intermediate type ($p = 0.005$) for the total sample and the SUD + SZ group compared to intermediate type and morning type ($p < 0.001$, in both cases).

Table 3
Chronotype percentages for the groups of SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) and statistical contrast (Chi-Square test).

	SUD (N = 80)	SUD + SZ (N = 75)	Statistical contrast
Evening type	27.5%	58%	χ^2_1=7.333**
Intermediate type	53.8%	25%	χ^2_1=9.290**
Morning type	18.8%	16%	χ^2_1=0.333

** $p < 0.01$.

Differences between groups were observed in bedtime during the workdays, and SUD group showed a delay of time to bed compared with SUD + SZ ones ($p = 0.007$). That is to say, SUD ones went to bed later than SUD + SZ patients during the workdays. Results confirmed the same considering age and age of SUD onset as covariates (see Table 4). Moreover, although the stability of sleep schedules was greater in the SUD + SZ group, no relevant SJL is observed in either group.

Regarding to PSQI components, only a significant difference was observed in sleep medication between SUD and SUD + SZ groups ($p = 0.032$). SUD patients reported lower consumption while SUD + SZ ones had more frequency of prescribed drugs to sleep during the last month (see Table 5). There was no significant difference between the two groups in other dimensions of PSQI scale nor in the total PSQI scores. However, it is worth noting the high number of patients with a sleep efficiency lower than 65% (half of the SUD and more than a third of the SUD + SZ group), sleep disturbances one or more times a week (more than a third in both groups) and that day time dysfunction is a somewhat or very large problem in about 40% of patients regardless of the

Table 4
Social jet-lag and related parameters for the SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) groups. Mean scores ± standard deviation, F and partial eta square (η^2_p) (MANCOVA results).

			Age as covariate		Age and age of SUD onset as covariates	
	SUD (N = 80)	SUD + SZ (N = 75)	$F_{(1,152)}$	η^2_p	$F_{(1,151)}$	η^2_p
Bedtime during the workdays	00.28 ± 1.51	23.42 ± 1.57	7.564**	0.047	5.090*	0.026
Wake up during the workdays	7.38 ± 1.45	7.40 ± 1.42	0.503	0.003	1.181	0.006
Bedtime during the free days	00.41 ± 2.16	00.15 ± 1.46	1.570	0.010	0.724	0.004
Wake up during the free days	8.46 ± 1.59	9.03 ± 2.03	2.880	0.012	3.077	0.013
Social jet-lag	1.13 ± 2.55	0.46 ± 0.59	1.304	0.008	1.426	0.011

* $p < 0.05$;
** $p < 0.01$.

Table 5
Quality and dimensions of sleep for the SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) patients. Percentage and statistical contrast (Chi-Square test).

PSQI	SUD (N = 80)	SUD + SZ (N = 75)	Statistical contrast
Sleep quality			x^2_3= 1.765
Very good	17.2%	16%	x^2_1= 0.062
Fairly good	53.6%	45.3%	x^2_1=1.102
Fairly bad	17.5%	22.6%	x^2_1=0.640
Very bad	11.3%	16%	x^2_1=0.739
Sleep latency			x^2_3=4.051
Lower than 15 min	56.8%	42.7%	x^2_1=3.496
16–30 min	21.3%	32%	x^2_1=2.310
31–60 min	17.5%	18.7%	x^2_1=0.036
>60 min	3.8%	6.7%	x^2_1=0.656
Sleep duration			x^2_3=3.565
>7 h	8.8%	6.7%	x^2_1=0.240
6–7 h	35%	49.3%	x^2_1=3.312
5–6 h	44.4%	37.3%	x^2_1=0.940
<5 h	11.3%	6.7%	x^2_1=1.020
Sleep efficiency			x^2_3=4.327
>85%	21%	24%	x^2_1=0.168
75%–84%	4%	2.7%	x^2_1=0.144
65%–74%	24.7%	37.3%	x^2_1=2.788
Lower than 65%	49.4%	36%	x^2_1=3.168
Sleep disturbance			x^2_3=0.882
Not during past month	5%	6.1%	x^2_1=0.193
Less than once a week	61.3%	54.7%	x^2_1=0.688
Once or twice a week	31.3%	34.7%	x^2_1=0.202
Three or more times a week	2.5%	4%	x^2_1=0.270
Sleep medication			x^2_3=8.805*
Not during past month	43.2%	25.3%	x^2_1=6.051*
Less than once a week	9.9%	8%	x^2_1=0.193
Once or twice a week	28.4%	29.3%	x^2_1=0.062
Three or more times a week	18.5%	37.3%	x^2_1=6.864*
Daytime dysfunction			x^2_3=4.651
No problem at all	32.5%	21.3%	x^2_1=2.496
Only a very slight problem	26.3%	40%	x^2_1=3.348
Somewhat of a problem	32.1%	33.3%	x^2_1=0.012
A very big problem	9%	5.3%	x^2_1=0.705

PSQI: Pittsburgh sleep quality index.
* $p < 0.05$.

diagnosis group. Finally, analyses indicated no interaction between chronotype and group in total PSQI scores.

3.3. Quality of life

The mean scores for all dimensions of WHOQOL-BREF were lower in the group of SUD + SZ patients in comparison with Iranian population norms ($t_{979} > 9.720, p < 0.001$) (Nedjat et al., 2008). The dimensions of Physical health, Psychological health and Social Relationship of SUD group also scored lower than norms (t_{984}= 3.04, $p < 0.002$, in all cases); just only the Environmental health of this group was similar to the norm (t_{984}= 1.100, $p = 0.271$). See Fig. 1.

Results on dimensions of WHOQOL-BREF presented the highest scores in SUD patients compared to SUD + SZ ones; explaining in Physical health ($p = 0.001$), Psychological health ($p = 0.013$), Social relationship ($p < 0.001$), and Environmental health ($p < 0.001$). Moreover, for the overall QOL, SUD patients also presented the highest scores compared to SUD + SZ patients ($p = 0.001$). The second MANCOVA analysis considering age and age of onset of SUD as covariates displayed the same results. See Table 6.

Multiple regression analysis of QOL and its dimensions scales related to clinical variables indicated that in SUD + SZ group, both previous suicide attempts and SJL were negatively related to Physical health, explaining 10.3% of the variance in this dimension ($F_{(2,72)} = 5.226; p < 0.01$). Also, the score of PANSS was negatively related to Psychological health explaining 5.5% of its variance ($F_{(1,73)} = 5.275; p < 0.05$). Previous suicide attempts and PANSS were negatively related to Social relationship, explaining 16.4% of its variance ($F_{(2,72)} = 8.280; p < 0.01$). Moreover, in the SUD + SZ group, SJL was negatively related to overall QOL, explaining 8.2% of its variance ($F_{(1,73)} = 7.600; p < 0.01$). No variables were associated with WOQOL-BREF dimensions in SUD group or the total sample.

MANCOVA analysis was used to examine the differences between levels of PSQI dimensions on QOL dimensions. This analysis showed no interaction between sleep quality and groups in Physical health, Environmental health and overall QOL. While in the Psychological health an interaction between sleep quality and group ($F_{(3146)} = 3.690; \eta^2_p = 0.070; p = 0.013$) was obtained, the patients with higher sleep quality reported more Psychological health (62.79 ± 20.44) compared to very bad ones (36.25 ± 18.89) in the SUD group. Regarding the total sample, the main effect of sleep quality appears significant in Physical health ($F_{(3146)} = 7.400; \eta^2_p = 0.132; p < 0.001$); the patients who reported very good sleep quality had higher Physical health (53.29 ± 19.08) compared to very bad ones (37.50 ± 17.24). Also, a significant difference was observed between sleep quality levels in Environmental health ($F_{(3146)} = 3.033; \eta^2_p = 0.059; p = 0.031$). The patients who reported very good sleep quality had higher Environmental health (51.92 ± 20.58) compared to very bad ones (39.01 ± 19.09). Moreover, a significant difference was observed between sleep quality levels in overall QOL ($F_{(3146)} = 4.566; \eta^2_p = 0.086; p = 0.004$); the patients who reported very good sleep quality had higher overall QOL score (53.84 ± 23.91) compared to very bad ones (43.18 ± 25.21). There was no evidence of significant difference in the Social relationship dimension.

MANCOVA analysis used to establish the differences between sleep latency in QOL exhibited no interaction in overall QOL, Psychological health and Social relationship. Therefore, the main effect in the total sample showed a significant difference among sleep latency levels in these variables. In the overall QOL ($F_{(3146)} = 4.302; \eta^2_p = 0.081; p = 0.006$) the patients who reported lower that 15 min of sleep latency reported higher scores (64.06 ± 16.95) compared to those ones with >60 min of sleep latency (49.03 ± 23.30). In Psychological, the main effect ($F_{(3146)} = 3.897; \eta^2_p = 0.074; p = 0.01$) showed that the patients who reported lower than 15 min of sleep latency reported higher Psychological health (49.62 ± 19.82) compared to those ones with >60 min of sleep latency (45.83 ± 16.96). Also, the main effect of Social relationship ($F_{(3146)} = 5.586; \eta^2_p = 0.103; p = 0.001$) indicated that the patients who reported >60 min of sleep latency had lower Social relationship (51.28 ± 23.83) compared to those with lower than 15 min of sleep latency (67.70 ± 14.39). There was no evidence of a significant difference in other dimensions of QOL. Correlations between scores of QOL and PSQI also revealed a negative link between them ($\rho = -0.181$, $p = 0.024$), suggesting that patients with better quality of sleep reported a better QOL. The correlation performed for each clinical group did not provide differences in any of them. Likewise, adding chronotype as a factor in MANCOVA analysis revealed no significant differences nor for their interaction with group in QOL scale.

4. Discussion

This study concentrated on the characteristics and probable differences in the clinical state of male SUD and SUD + SZ patients under treatment, along with their circadian functioning (chronotype, SJL and quality of sleep) and QOL. Moreover, for chronotype and QOL we

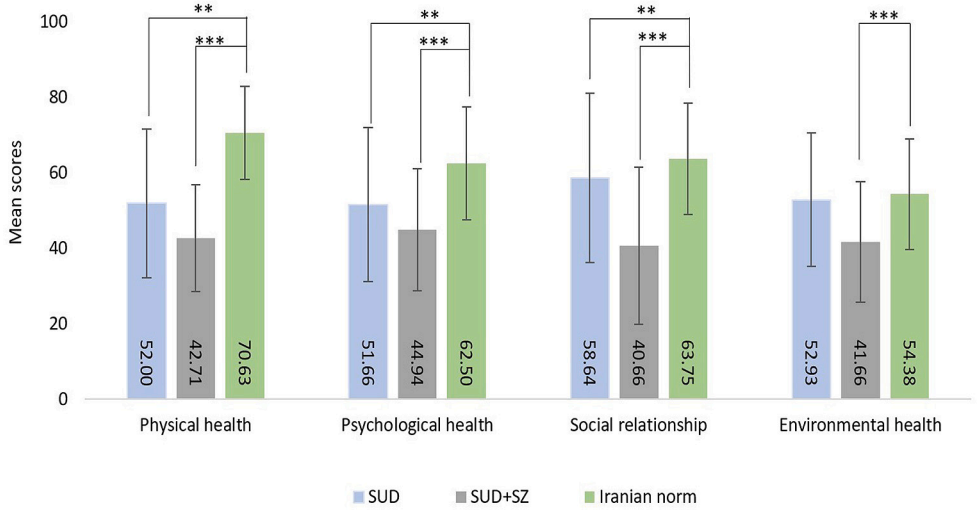


Fig. 1. Mean and standard deviations for the dimensions of quality of life in SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia) groups compared to Iranian population norms. $^{**}p < 0.01$; $^{***}p < 0.001$.

Table 6
Quality of life (QOL) results in the groups of SUD (substance use disorder) and SUD + SZ (substance use disorder comorbid schizophrenia). Mean scores, standard deviation, F and partial eta square (η_p^2) tests (MANCOVA results).

			Age as covariate		Age and age of onset of SUD as covariates	
WHOQOL-BREF	SUD (N = 80)	SUD + SZ (N = 75)	$F_{(1,152)}$	η_p^2	$F_{(1,151)}$	η_p^2
Overall QOL	52.34 ± 23.54	41.50 ± 20.46	10.558**	0.065	9.525**	0.059
Physical health	52.00 ± 19.68	42.71 ± 14.23	11.471**	0.070	8.757**	0.055
Psychological health	51.66 ± 20.35	44.94 ± 16.22	6.320*	0.040	4.110*	0.026
Social relationship	58.64 ± 22.44	40.66 ± 20.86	28.605***	0.158	25.039***	0.142
Environmental health	52.93 ± 17.74	41.66 ± 15.96	17.853***	0.105	15.208***	0.091

WHOQOL-BREF: Shortened version of the World Health Organization's Quality of Life Questionnaire;
* $p < 0.05$;
** $p < 0.01$;
*** $p < 0.001$.

compared our data with population norms and detect clinical correlates of sleep and circadian rhythmicity characteristics of each group.

Concerning the sociodemographic characteristics, our study is in agreement with previous research confirming that SUD + SZ patients under treatment are younger compared with those with a single disorder (Addington and Addington, 2007; Marquez-Arrico et al., 2019; Wobrock et al., 2013) or other dual disorder ones (Higgs et al., 2020; Serrano-Serrano et al., 2021). SUD + SZ group exhibited lower academic degrees compared with the SUD group (Serrano-Serrano et al., 2021), suggesting the possible presence already in the premorbid phase of a more problematic functioning and personality traits (Prat et al., 2021) which are related to loss of social support (Adan et al., 2017a; Marquez-Arrico et al., 2015) and might be considered an obstacle to academic development in dual patients. Regarding the clinical state, SUD + SZ patients presented a younger age of SUD onset, more previous psychiatric history and daily use of medication compared with SUD which has been reported previously (Addington and Addington, 2007; Benaiges et al., 2013; Marquez-Arrico et al., 2019; Río-Martínez et al., 2020; Serrano-Serrano et al., 2021). This could be related to more maladaptive coping strategies (Adan et al., 2017a; Marquez-Arrico et al., 2015; Marquez-Arrico et al., 2019) or personality traits (Huber et al., 2016; Marquez-Arrico and Adan, 2016; Oh et al., 2021) such as more impulsivity or less sociability observed in SUD + SZ patients as compared to single disorders (SZ or SUD).

Notwithstanding the limited number of studies on circadian functioning and its characteristics in dual patients, our data showed the most prevalent chronotype was the evening type in SUD + SZ and the intermediate type in SUD despite being in early remission phase in an intensive treatment. We found a novel fact that should be emphasized, namely, the highest rate of polydrug users were reported to be evening type in both SUD + SZ group and the total sample, in line with previous findings indicating a high probability to use more substances in evening type individuals (Ghaseminejad et al., 2015; Kervran et al., 2015; Prat and Adan, 2011) and in SUD + SZ compared to SUD (Adan et al., 2017a; Luca and Peris, 2020; Marquez-Arrico et al., 2015; Río-Martínez et al., 2020). There is evidence that the evening pattern of patients hinders the response to SUD treatment (Adan, 2013; Adan et al., 2012; Ghaseminejad et al., 2015) and the remission of psychotic symptoms (Kaskie et al., 2017; Waite et al., 2016; Wilson and Argyropoulos, 2012). It should be noted that patients in both groups do not show problematic social jet-lag (≥2 h), their sleep schedules are quite regular and most of them sleep enough hours, however SUS + SZ patients reported a higher amount of sleep medication. It seems substance use, regardless of the mental disorder, can impact circadian rhythms with a detriment in sleep (lower efficiency and sleep disturbances) and also in the diurnal period with lower activation (Capella et al., 2018; Serrano-Serrano et al., 2021). Our study suggests that this seems detectable with the chronotype assessment for patients already enrolled in treatment. Therefore, a chronobiological approach to modify the levels of daily activity in the social-work timetable and time adjustments in habits towards the morningness pattern (Adan, 2013; Kaskie et al., 2017; Wittmann et al., 2006) in SUD with and without comorbid SZ is recommended.

Although few studies have been done on the QOL of SUD + SZ patients, we observed worse scores in SUD + SZ patients than SUD ones in

line with previous findings (Aras et al., 2013; Benaiges et al., 2012). Possible reasons include that SUD + SZ patients have greater difficulties in asking for support, lower social network, making friends (Marquez-Arrico et al., 2015), and consequently a more stressful life associated with daily conflicts (Aras et al., 2013) with lower vitality, social functions and emotional roles (Adan et al., 2017b), which may lead to higher suicide attempts (Adan et al., 2017a; Huber et al., 2016; Río-Martínez et al., 2020). The majority of the studies reported worse QOL among SUD + SZ patients, although it could be related to the long-term use of substances (Benaiges et al., 2013; Adan et al., 2017a). Recent data suggest that SUD + SZ patients have greater cognitive reserve (Herrero et al., 2020) and social premorbid functioning (Prat et al., 2021) than SZ patients, which points to a lower vulnerability to the impairment of SZ. In this sense, longitudinal studies assessing the impact of age related to consumption in SUD and SUD + SZ patients are needed.

We found that previous suicide attempts were negatively related to the Physical health of the SUD + SZ group. SJL was negatively linked to Psychological health and overall QOL of the SUD + SZ group. Moreover, more severity of SZ was related to the lower Psychological health of these patients. Also, previous suicide attempts and severity of SZ were negatively related to the Social relationship of the SUD + SZ group. These results extended previous results on SUD + SZ and SZ patients in which a relationship was found between current suicide risk, and first-degree relatives with SUD, insight and positive symptoms (Adan et al., 2017a), body pain and SZ severity (Adan et al., 2017b) and impaired clinical and psychosocial adjustments with lower QOL (Carra et al., 2016). Health-related studies reported associations between QOL and severity of SUD (Adan et al., 2017b; Carra et al., 2016) and treatment duration in psychotic patients (Desalegn et al., 2020; Drake et al., 2020). Adherence to treatment has been observed to improve the QOL of SUD + SZ (Drake et al., 2006; Margolese et al., 2006; Wojtalik and Eack, 2019), SZ (Costa et al., 2018; Wilson and Argyropoulos, 2012) and SUD patients (Giménez-Meseguer et al., 2015), especially in the Physical and Psychological health, Vitality, Social function, and General health perception, although more research is required in this area.

An interesting relationship between more sleep quality and better overall QQL (overall, Psychological, Physical and Environmental health) for the total sample was found. In addition, patients with more sleep latency reported lower Social relationship, Psychological health and overall QOL. Our results extend to the diagnoses we have examined the previous findings on SZ patients that worse QOL is related with poorer sleep quality (Brissos et al., 2013; Hofstetter et al., 2005; Xiang et al., 2009). In this line, it is important to highlight that physical activity can improve the sleep quality in SUD (Adan, 2013) and SZ patients (Costa et al., 2018) as a beneficial non-pharmacological intervention, being able to be extensible to SUD + SZ patients. Given that SZ patients may have worse family support and lower QOL compared to good sleepers, and having suggested that considering family support and sleep hygiene programs in their treatment may have high pros points (Brissos et al., 2013), the potential benefit of applying it also in SUD + SZ should be investigated in the future. All previous studies underline the importance of paying attention to QOL of SUD, SZ or SUD + SZ patients, emphasizing related factors, in particular the sleep quality. Therefore, since the QOL of dual patients related to their circadian functioning has received less attention up to now, future therapeutic approaches should considerer in-depth to this scope and its improvement of the clinical populations, SUD and dual disorder ones, especially SUD + SZ patients.

Our study has some limitations such as non-randomized groups without a control group. It is the first study in this scope in Iran so our results can be not generalized to other mental disorders or other countries, but the similarities found despite the cultural differences in the substances used bring us closer to the consideration of a worldwide phenomenon. Only the male gender was investigated, therefore it is recommended to take into account also female gender in future works. Preferably, patients should be included at the time they access the resource requesting treatment for SUD and measurements should be scheduled at various times during treatment, including objective records of circadian rhythmicity and sleep (i.e. actigraphy, type and intensity of light exposure). A strength of our study was to have provided for the first-time new insights to previous research exploring both circadian functioning and QOL in SUD patients with and without comorbid SZ, as well as an accurate diagnosis and an exhaustive evaluation of clinical characteristics with a large number of patients in each group.

5. Conclusion

This work has focused on the circadian functioning and QOL in SUD patients with and without comorbid SZ. Regarding chronotype, we found that polydrug and SUD + SZ patients were more prone to evening type. SUD patients reported later bedtime on workdays, however patients in both groups did not show a problematic SJL or differences in sleep quality although SUD + SZ patients took more sleep medication. These findings suggest, in line with previous studies, that QOL of dual patients is worse than in normative population and in SUD patients. This study provides new insight into a negative relation between SZ severity, SJL, suicide attempts with Physical health, Psychological health and Social relationship in the SUD + SZ group. Our results illustrate the importance of pay attention to circadian characteristics and QOL of clinical populations such as SUD with and without SZ. We hope that this work sparks an effective approach for further research to focus on ways to improve the lifestyle of the groups of patients studied, overcoming the limitations mentioned, in order to achieve better and more effective treatment protocols.

Funding

This research was funded by the grant PID2020-117767GB-I00 of Spanish Ministry of Science and Innovation (MCIN/AEI/https://doi.org/10.13039/501100011033) and the Generalitat de Catalunya (2017SGR-748).

Data availability

The data presented in this study are available on reasonable request from the corresponding author.

Authors contributions

AA conceptualized and designed the study. IH was for responsible data of acquisition and curation. IH and AA analyzed and interpreted the data. IH and AA wrote the manuscript and JFN critically reviewed the manuscript text. All authors read and approved the final manuscript.

Ethical statement

This study was approved by the ethics committee of the Research Committee of the University of Barcelona (IRB00003099) and authorization from the research center of Shiraz University of medical science was also obtained.

Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgements

We would like to express our special thanks to the dear management of the psychiatric center, Dr. I. Hashemzadeh, and the addiction treatment center, Dr. h. Kushesh who give us the opportunity to do this

project. We are thankful to all of those patients who gave us their time and for their contributions to complete the work.

References

Adan, A., 2013. A chronobiological approach to addiction. J. Subst Use 18 (3), 171–183. https://doi.org/10.3109/14659891.2011.632060.

Adan, A., Almirall, H., 1991. Horne & Östberg morningness-eveningness questionnaire: a reduced scale. Pers. Individ. Differ 12 (3), 241–253. https://doi.org/10.1016/0191-8869(91)90110-W.

Adan, A., Torrens, M., 2021. Diagnosis and Management of Addiction and Other Mental Disorders (Dual Disorders). J. Clin. Med 10 (6), 1307. https://doi.org/10.3390/jcm10061307. Vol. 10. Multidisciplinary Digital Publishing Institute, pp. 1–4.

Adan, A., Archer, S.N., Hidalgo, M.P., Di Milia, L., Natale, V., Randler, C., 2012. Circadian typology: a comprehensive review. Chronobiol Int 29 (9), 1153–1175. https://doi.org/10.3109/07420528.2012.719971.

Adan, A., Capella, M.d.M, Prat, G., Forero, D.A., López-Vera, S., Navarro, J.F., 2017a. Executive functioning in men with schizophrenia and substance use disorders. Influence of lifetime suicide attempts. PLoS One 12 (1). https://doi.org/10.1371/journal.pone.0169943.

Adan, A., Marquez-Arrico, J.E., Gilchrist, G., 2017b. Comparison of health-related quality of life among men with different co-existing severe mental disorders in treatment for substance use. Health Qual. Life Outcomes 15 (1), 1–12. https://doi.org/10.1186/s12955-017-0781-y.

Addington, J., Addington, D., 2007. Patterns, predictors and impact of substance use in early psychosis: a longitudinal study. Acta Psychiatr. Scand. 115 (4), 304–309. https://doi.org/10.1111/j.1600-0447.2006.00900.x.

Afonso, P., Figueira, M.L., Paiva, T., 2014. Sleep–wake patterns in schizophrenia patients compared to healthy controls. World J. Biol. Psychiatry 15 (7), 517–524.

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). American Psychiatric Pub.

Aras, H.I., Yazar, M.S., Altinbas, K., 2013. Quality of life among dually diagnosed and non-substance-using male schizophrenia outpatients. S Afr. J. Phychiatr 19 (2), 35–39.

Benaiges, I., Prat, G., Adan, A., 2012. Health-related quality of life in patients with dual diagnosis: clinical correlates. Health Qual. Life Outcomes 10, 106. https://doi.org/10.1186/1477-7525-10-106.

Benaiges, I., Serra-Grabulosa, J.M., Adan, A., 2013. Neuropsychological functioning and age-related changes in schizophrenia and/or cocaine dependence. Prog Neuropsychopharm & Biol Psychiatr 40, 298–305. https://doi.org/10.1016/j.pnpbp.2012.10.016.

Bollu, P.C., Kaur, H., 2019. Sleep medicine: insomnia and sleep. Mo. Med. 116 (1), 68–75.

Bootzin, R.R., Stevens, S.J., 2005. Adolescents, substance abuse, and the treatment of insomnia and daytime sleepiness. Clin 25 (5), 629–644. https://doi.org/10.1016/j.cpr.2005.04.007.

Brissos, S., Afonso, P., Cañas, F., Bobes, J., Bernardo Fernandez, I., Guzman, C., 2013. Satisfaction with life of schizophrenia outpatients and their caregivers: differences between patients with and without self-reported sleep complaints. Schizophr Res Treat 2013. https://doi.org/10.1155/2013/502172.

Brunette, M.F., Mueser, K.T., Babbin, S., Meyer-Kalos, P., Rosenheck, R., Correll, C.U., Cather, C., Robinson, D.G., Schooler, N.R., Penn, D.L., 2018. Demographic and clinical correlates of substance use disorders in first episode psychosis. Schizophr 194, 4–12. https://doi.org/10.1016/j.schres.2017.06.039.

Capella, M.d.M., Martinez-Nicolas, A., Adan, A., 2018. Circadian rhythmic characteristics in men with substance use disorder under treatment. Influence of age of onset of substance use and duration of abstinence. Front Psychiatry 9, 373. https://doi.org/10.3389/fpsyt.2018.00373.

Carra, G., Johnson, S., Crocamo, C., Angermeyer, M.C., Brugha, T., Azorin, J.-M., Toumi, M., Bebbington, P.E., 2016. Psychosocial functioning, quality of life and clinical correlates of comorbid alcohol and drug dependence syndromes in people with schizophrenia across Europe. Psychiatry Res. 239, 301–307. https://doi.org/10.1016/j.psychres.2016.03.038.

Chakravorty, S., Vandrey, R., He, S., Stein, M.D., 2018. Sleep management among patients with substance use disorders. Med. Clin. North Am 102 (4), 733–743. https://doi.org/10.1016/j.mcna.2018.02.012.

Chang, S.J., Jang, S.J., 2019. Social jetlag and quality of life among nursing students: a cross-sectional study. J. Adv. Nurs. 75 (7), 1418–1426. https://doi.org/10.1111/jan.13857.

Chen, L., Selvendra, A., Stewart, A., Castle, D., 2018. Risk factors in early and late onset schizophrenia. Compr Psychiatry 80, 155–162. https://doi.org/10.1111/jan.13857.

Chen, Z.T., Wang, H.T., Chueh, K.H., Liu, I.C., Yang, C.M., 2021. An exploration of the sleep quality and potential violence among patients with schizophrenia in community. Perspect Psychiatr Care 57 (2), 648–654. https://doi.org/10.1111/ppc.12589.

Chung, K.-F., Poon, Y.P.Y.-P., Ng, T.-K., Kan, C.-K., 2018. Correlates of sleep irregularity in schizophrenia. Psychiatry Res. 270, 705–714. https://doi.org/10.1016/j.psychres.2018.10.064.

Costa, R., Bastos, T., Probst, M., Seabra, A., Vilhena, E., Corredeira, R., 2018. Sleep quality in patients with schizophrenia: the relevance of physical activity. Ment. Health Phys. Act. 14, 140–145. https://doi.org/10.1016/j.mhpa.2018.04.004.

Daigre, C., Grau-López, L., Rodríguez-Cintas, L., Ros-Cucurull, E., Sorribes-Puertas, M., Esculies, O., Bones-Rocha, K., Roncero, C., 2017. The role of dual diagnosis in health-related quality of life among treatment-seeking patients in Spain. Qual. Life Res. 26 (12), 3201–3209. https://doi.org/10.1007/s11136-017-1668-4.

Desalegn, D., Girma, S., Abdeta, T., 2020. Quality of life and its association with current substance use, medication non-adherence and clinical factors of people with schizophrenia in Southwest Ethiopia: a hospital-based cross-sectional study. Health Qual. Life Outcomes 18 (1), 1–9. https://doi.org/10.1186/s12955-020-01340-0.

Donoghue, K., Doody, G.A., Murray, R.M., Jones, P.B., Morgan, C., Dazzan, P., Hart, J., Mazzoncini, R., MacCabe, J.H., 2014. Cannabis use, gender and age of onset of schizophrenia: data from the AESOP study. Psychiatry Res. 215 (3), 528–532. https://doi.org/10.1016/j.psychres.2013.12.038.

Drake, R.E., McHugo, G.J., Xie, H., Fox, M., Packard, J., Helmstetter, B., 2006. Ten-year recovery outcomes for clients with co-occurring schizophrenia and substance use disorders. Schizophr 32 (3), 464–473. https://doi.org/10.1093/schbul/sbj064.

Drake, R.E., Xie, H., McHugo, G.J., 2020. A 16-year follow-up of patients with serious mental illness and co-occurring substance use disorder. World Psychiatry 19 (3), 397. https://doi.org/10.1002/wps.20793.

Galván, A., 2020. The need for sleep in the adolescent brain. Trends Cogn. Sci. 24 (1), 79–89. https://doi.org/10.1016/j.tics.2019.11.002.

Ghaseminejad, M.A., Purgholami, F., Sadrmohamadi, R., 2015. Simple and Multiple Relationships between morningness/eveningness orientation, anxiety sensitivity and addiction in university students. J. Appl. Behav 2 (2), 1–6. https://doi.org/10.22037/ijabs.v2i2.7509.

Giménez-Meseguer, J., Tortosa-Martínez, J., Remedios Fernández-Valenciano, M., 2015. Benefits of exercise for the quality of life of drug-dependent patients. J. Psychoactive Drugs 47 (5), 409–416. https://doi.org/10.1080/02791072.2015.1102991.

Hashemzadeh, I., Marquez-Arrico, J.E., Hashemzadeh, K., Navarro, J.F., Adan, A., 2021. Circadian functioning and quality of life in substance use disorder patients with and without comorbid major depressive disorder. Front. Psychiatry 1844. https://doi.org/10.3389/fpsyt.2021.750500.

Herrero, P., Contador, I., Stern, Y., Fernández-Calvo, B., Sánchez, A., Ramos, F., 2020. Influence of cognitive reserve in schizophrenia: A systematic review. Neurosci. Biobehav. Rev. 108, 149–159. https://doi.org/10.1016/j.neubiorev.2019.10.019.

Higgs, P., Piri, N., Sadri, E., Pourghasem, M., Fakhari, S.J., Noroozi, M., Miladinia, M., Mousavi, S.B., 2020. Prevalence of substance use among psychiatric patients with psychosis and determining its strongest predictor. Res. Sq. https://doi.org/10.21203/rs.2.21050/v1.

Hofstetter, J.R., Lysaker, P.H., Mayeda, A.R., 2005. Quality of sleep in patients with schizophrenia is associated with quality of life and coping. BMC Psychiatry 5 (1), 1–5. https://doi.org/10.1186/1471-244X-5-13.

Huber, C.G., Hochstrasser, L., Meister, K., Schimmelmann, B.G., Lambert, M., 2016. Evidence for an agitated-aggressive syndrome in early-onset psychosis correlated with antisocial personality disorder, forensic history, and substance use disorder. Schizophr 175 (1–3), 198–203. https://doi.org/10.1016/j.schres.2016.04.027.

Juel, A., Kristiansen, C.B., Madsen, N.J., Munk-Jørgensen, P., Hjorth, P., 2017. Interventions to improve lifestyle and quality-of-life in patients with concurrent mental illness and substance use. Nord. J. Psychiatry 71 (3), 197–204. https://doi.org/10.1080/08039488.2016.1251610.

Kaskie, R.E., Graziano, B., Ferrarelli, F., 2017. Schizophrenia and sleep disorders: links, risks, and management challenges. Nat. Sci. Sleep 9, 227–239. https://doi.org/10.2147/NSS.S121076.

Kervran, C., Fatséas, M., Serre, F., Taillard, J., Beltran, V., Leboucher, J., Debrabant, R., Alexandre, J.-M., Daulouède, J.-P., Philip, P., 2015. Association between morningness/eveningness, addiction severity and psychiatric disorders among individuals with addictions. Psychiatry Res. 229 (3), 1024–1030. https://doi.org/10.1016/j.psychres.2015.05.026.

Kivelä, L., Papadopoulos, M.R., Antypa, N., 2018. Chronotype and psychiatric disorders. Curr. Sleep Med. Rep. 4 (2), 94–103. https://doi.org/10.1007/s40675-018-0113-8.

Klingaman, E.A., Palmer-Bacon, J., Bennett, M.E., Rowland, L.M., 2015. Sleep disorders among people with schizophrenia: emerging research. Curr. Psychiatry Rep. 17 (10), 1–8. https://doi.org/10.1007/s11920-015-0616-7.

Korenic, S.A., Klingaman, E.A., Wickwire, E.M., Gaston, F.E., Chen, H., Wijtenburg, S.A., Rowland, L.M., 2020. Sleep quality is related to brain glutamate and symptom severity in schizophrenia. J. Psychiatry 120, 14–20. https://doi.org/10.1016/j.jpsychires.2019.10.006.

Laskemoen, J.F., Simonsen, C., Büchmann, C., Barrett, E.A., Bjella, T., Lagerberg, T.V., Vedal, T.J., Andreassen, O.A., Melle, I., Aas, M., 2019. Sleep disturbances in schizophrenia spectrum and bipolar disorders–a transdiagnostic perspective. Compr Psychiatry 91, 6–12. https://doi.org/10.1016/j.comppsych.2019.02.006.

Luca, G., Peris, L., 2020. Sleep quality and sleep disturbance perception in dual disorder patients. J. Clin. Med. 9 (6), 2015. https://doi.org/10.3390/jcm9062015.

Margolese, H.C., Negrete, J.C., Tempier, R., Gill, K., 2006. A 12-month prospective follow-up study of patients with schizophrenia-spectrum disorders and substance abuse: changes in psychiatric symptoms and substance use. Schizophr 83 (1), 65–75. https://doi.org/10.1016/j.schres.2005.11.019.

Marquez-Arrico, J.E., Adan, A., 2016. Personality in patients with substance use disorders according to the co-occurring severe mental illness: a study using the alternative five factor model. Pers. Individ. Differ. 97, 76–81. https://doi.org/10.1016/j.paid.2016.03.028.

Marquez-Arrico, J.E., Benaiges, I., Adan, A., 2015. Strategies to cope with treatment in substance use disorder male patients with and without schizophrenia. Psychiatry Res. 228 (3), 752–759. https://doi.org/10.1016/j.psychres.2015.05.028.

Marquez-Arrico, J.E., Río-Martínez, L., Navarro, J.F., Prat, G., Forero, D.A., Adan, A., 2019. Coping strategies in male patients under treatment for substance use disorders and/or severe mental illness: influence in clinical course at one-year follow-up. J. Clin. Med. 8 (11), 1972. https://doi.org/10.3390/jcm8111972.

Moghaddam, J.F., Nakhaee, N., Sheibani, V., Garrusi, B., Amirkafi, A., 2012. Reliability and validity of the Persian version of the Pittsburgh sleep quality index (PSQI-P). Sleep Breath. 16 (1), 79–82. https://doi.org/10.1007/s11325-010-0478-5.

Murthy, P., Chand, P., 2012. Treatment of dual diagnosis disorders. Curr. Opin. Psychiatr. 25 (3), 194–200. https://doi.org/10.1097/YCO.0b013e328351a3e0.
Navid, S., Abolghasemi, A., Narimani, M., 2009. The relationship of emotional responses and positive and negative symptoms with quality of life in schizophrenic patients. GUMS 18 (71), 64–71.
Nedjat, S., Montazeri, A., Holakouie, K., Mohammad, K., Majdzadeh, R., 2008. Psychometric properties of the Iranian interview-administered version of the World Health Organization's Quality of Life Questionnaire (WHOQOL-BREF): a population-based study. BMC Health Serv. Res. 8 (1), 1–7. https://doi.org/10.1186/1472-6963-8-61.
Oh, H., Jang, S.-K., Lee, H.-S., Lee, E.-B., Choi, K.-H., 2021. Personality traits in individuals with the dual diagnosis of psychosis and substance use disorders: a comprehensive review and meta-analysis. J. Dual Diagn 17 (1), 34–51. https://doi.org/10.1080/15504263.2020.1839827.
Pan, Z., Zhang, J., Cheng, H., Bu, Q., Li, N., Deng, Y., Zhou, L., Dai, Z., Lyu, J., 2020. Trends of the incidence of drug use disorders from 1990 to 2017: an analysis based on the Global Burden of Disease 2017 data. Epidemiology Psychiatric Sci. vol. 29, e148. https://doi.org/10.1017/S2045796020000657.
Prat, G., Adan, A., 2011. Influence of circadian typology on drug consumption, hazardous alcohol use, and hangover symptoms. Chronobiol. Int 28 (3), 248–257. https://doi.org/10.3109/07420528.2011.553018.
Prat, G., Marquez-Arrico, J.E., Río-Martínez, L., Navarro, J.F., Adan, A., 2021. Premorbid functioning in schizophrenia spectrum disorders with comorbid substance use: A systematic review. Prog. Neuropsychopharmacol & Biol Psychiatr 110, 110310. https://doi.org/10.1016/j.pnpbp.2021.110310.
Pritchett, D., Wulff, K., Oliver, P.L., Bannerman, D.M., Davies, K.E., Harrison, P.J., Peirson, S.N., Foster, R.G., 2012. Evaluating the links between schizophrenia and sleep and circadian rhythm disruption. J. Neural Transm. 119 (10), 1061–1075. https://doi.org/10.1007/s00702-012-01817-8.
Rahafar, A., Meysam, S.J., Sadeghpour, A., Heidari, Z., Kasaeian, A., 2015a. Psychometric properties of the Persian version of the reduced Morningness-Eveningness questionnaire: further evidence. Sleep Biol. Rhythms 13 (2), 112–116. https://doi.org/10.1111/sbr.12093.
Rahafar, A., Meysam, S.J., Sadeghpour, A., Heidari, Z., Kasaeian, A., 2015b. Psychometric properties of the Persian version of the reduced Morningness-Eveningness Questionnaire: further evidence. Sleep Biol. Rhythms 13 (2), 112–116. https://doi.org/10.1111/sbr.12093.
Reeve, S., Sheaves, B., Freeman, D., 2019. Sleep disorders in early psychosis: incidence, severity, and association with clinical symptoms. Schizophr. Bull. 45 (2), 287–295. https://doi.org/10.1093/schbul/sby129.
Río-Martínez, L., Marquez-Arrico, J.E., Prat, G., Adan, A., 2020. Temperament and character profile and its clinical correlates in male patients with dual schizophrenia. J. Clin. Med. 9 (6), 1876. https://doi.org/10.3390/jcm9061876.
Robertson, I., Cheung, A., Fan, X., 2019. Insomnia in patients with schizophrenia: current understanding and treatment options. Prog. Neuropsychopharmacol & Biol Psychiatr 92, 235–242. https://doi.org/10.1016/j.pnpbp.2019.01.016.
Roenneberg, T., 2012. What is chronotype? Sleep Biol. Rhythms 10 (2), 75–76. https://doi.org/10.1111/j.1479-8425.2012.00541.x.
Serrano-Serrano, A.B., Marquez-Arrico, J.E., Navarro, J.F., Martinez-Nicolas, A., Adan, A., 2021. Circadian characteristics in patients under treatment for substance use disorders and severe mental illness (schizophrenia, major depression and bipolar sisorder). J. Clin. Med. 10 (19), 4388. https://doi.org/10.3390/jcm10194388.
Sharma, P., Dikshit, R., Shah, N., Karia, S., De Sousa, A., 2016. Excessive daytime sleepiness in schizophrenia: a naturalistic clinical study. J. Clin. Diagn. Res. 10 (10), VC06. https://doi.org/10.7860/JCDR/2016/21272.8627.
Talamo, A., Centorrino, F., Tondo, L., Dimitri, A., Hennen, J., Baldessarini, R., 2006. Comorbid substance-use in schizophrenia: relation to positive and negative symptoms. Schizophr 86 (1–3), 251–255. https://doi.org/10.1016/j.schres.2006.04.004.
Taylor, B.J., Bowman, M.A., Brindle, A., Hasler, B.P., Roecklein, K.A., Krafty, R.T., Matthews, K.A., Hall, M.H., 2020. Evening chronotype, alcohol use disorder severity, and emotion regulation in college students. Chronobiol. Int 37 (12), 1725–1735. https://doi.org/10.1080/07420528.2020.1800028.
Vetrova, M., Kuchmenko, D., Genina, I., Goncharov, O., Rybakova, K., Semenova, N., Zubova, E.Y., Kiselev, A., Neznanov, N., Krupitsky, E., 2020. The prevalence of the sleep disturbances among the patients with substance use disorders. Bull. Siberian Med. 18 (4), 26–35. https://doi.org/10.20538/1682-0363-2019-4-26-35.
Waite, F., Myers, E., Harvey, A.G., Espie, C.A., Startup, H., Sheaves, B., Freeman, D., 2016. Treating sleep problems in patients with schizophrenia. Behav. Cogn. Psychother. 44 (3), 273–287. https://doi.org/10.1017/S1352465815000430.
Wilkerson, A.K., Simmons, R.O., Sahlem, G.L., Taylor, D.J., Smith, J.P., Book, S.W., McRae-Clark, A.L., 2021. Sleep and substance use disorder treatment: a preliminary study of subjective and objective assessment of sleep during an intensive outpatient program. Am. J. Addict. https://doi.org/10.1111/ajad.13194.
Wilson, S., Argyropoulos, S., 2012. Sleep in schizophrenia: time for closer attention. Br. J. Psychiatry 200 (4), 273–274. https://doi.org/10.1192/bjp.bp.111.104091.
Wittmann, M., Dinich, J., Merrow, M., Roenneberg, T., 2006. Social jetlag: misalignment of biological and social time. Chronobiol. Int 23 (1–2), 497–509. https://doi.org/10.1080/07420520500545979.
Wittmann, M., Paulus, M., Roenneberg, T., 2010. Decreased psychological well-being in late 'chronotypes' is mediated by smoking and alcohol consumption. Subst. Use Misuse 45 (1–2), 15–30. https://doi.org/10.1080/07420520500545979.
Wobrock, T., Falkai, P., Schneider-Axmann, T., Hasan, A., Galderisi, S., Davidson, M., Kahn, R., Derks, E., Boter, H., Rybakowski, J., 2013. Comorbid substance abuse in first-episode schizophrenia: effects on cognition and psychopathology in the EUFEST study. Schizophr. Res 147 (1), 132–139. https://doi.org/10.1016/j.schres.2013.03.001.
Wojtalik, J.A., Eack, S.M., 2019. Cognitive enhancement therapy improves social relationships quality of life among individuals with schizophrenia misusing substances. Soc. Work. Res. 43 (1), 59–64. https://doi.org/10.1093/swr/svy032.
Wulff, K., Dijk, D.-J., Middleton, B., Foster, R.G., Joyce, E.M., 2012. Sleep and circadian rhythm disruption in schizophrenia. Br. J. Psychiatry 200 (4), 308–316. https://doi.org/10.1192/bjp.bp.111.096321.
Xiang, Y.-T., Weng, Y.-Z., Leung, C.-M., Tang, W.-K., Lai, K.Y., Ungvari, G.S., 2009. Prevalence and correlates of insomnia and its impact on quality of life in Chinese schizophrenia patients. Sleep 32 (1), 105–109. https://doi.org/10.5665/sleep/32.1.105.