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Substance Use and Sleep Problems in Patients With Psychotic Disorders

Erik Cederlöf[*,1,2,3], Minna Holm[1], Johan Ahti[2], Markku Lähteenvuo[4], Jarmo Hietala[5], Katja Häkkinen[6], Erkki Isometsä[2], Olli Kampman[7,8], Kaisla Lahdensuo[2], Jouko Lönnqvist[1], Jaana Suvisaari[1], Jari Tiihonen[4,9], Asko Wegelius[2], Juha Veijola[10,11,12], Aarno Palotie[6], Tuula Kieseppä[1,2], Solja Niemelä[5], and Tiina Paunio[1,2,3]

[1]Finnish Institute for Health and Welfare, Helsinki, Finland; [2]Department of Psychiatry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [3]SleepWell Research Program, Faculty of Medicine, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [4]Niuvanniemi Hospital, University of Eastern, Kuopio, Finland; [5]University of Turku, Turku, Finland; [6]Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland; [7]Faculty of Medicine and Health Technology, University of Tampere, Tampere, Finland; [8]Department of Psychiatry, University of Tampere, Tampere, Finland; [9]Karolinska Institutet, Solna, Sweden; [10]Department of Psychiatry, Oulu University Hospital, Oulu, Finland; [11]Department of Psychiatry, Research Unit of Clinical Neuroscience, University of Oulu, Oulu, Finland; [12]Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland

[*]To whom correspondence should be addressed; Finnish Institute for Health and Welfare, Population Health Unit, P.O. Box 30, FI-00271 Helsinki, Finland; tel: + 358-505731035, fax: +358 (0)29 524 6111, e-mail: erik.cederlof@thl.fi

***Background*: Substance use and sleep problems are common in patients with psychotic disorders, but their associations in these patients have not been evaluated. We aimed to investigate associations between substance use and sleep problems in a large nationwide cohort of patients with a psychotic disorder.*Study Design*: This study is part of the Finnish SUPER study, which belongs to the Stanley Global Neuropsychiatric Genomics Initiative. In this cross-sectional, multicenter study, participants (N = 8616) were recruited from primary and specialized healthcare. Patients with schizophrenia, schizoaffective disorder, bipolar disorder, and psychotic depression were included. Information on current alcohol (Alcohol Use Disorders Identification Test-Concise) and cigarette use as well as on lifetime illicit drug use, including cannabis, benzodiazepines, amphetamines, and opioids, was collected using questionnaires. The sleep outcomes in our logistic regression analysis were short (≤6 h) and long sleep (≥10 h) duration, difficulties initiating asleep, early morning awakenings, fatigue, and poor sleep quality (SQ).*Results*: Self-reported substance use was associated with a higher prevalence of sleep problems. After adjustments with age, gender, diagnostic group, and living status, hazardous alcohol use (eg, poor SQ odds ratio [OR] = 1.80, 95% CI: 1.49 to 2.16, P < .001), current smoking (short sleep duration OR = 1.28, 95% CI: 1.08 to 1.52, P = .005), and lifetime benzodiazepine misuse (difficulties initiating sleep OR = 2.00, 95% CI: 1.55 to 2.48, P < .001) were associated with sleep problems.*Conclusions*: Substance use was associated with sleep problems. Our findings underline the potential benefits of screening substance use when treating sleep problems in patients with psychotic disorders.**

Key words: insomnia/sleep/alcohol/smoking/illicit drugs

Introduction

Sleep problems are highly prevalent in patients with psychotic disorders.[1] The patients have both increased frequency of insomnia symptoms, such as difficulties initiating sleep (DIS), and early morning awakenings (EMAs), but also hypersomnia symptoms, with some patients simultaneously experiencing long sleep duration (long SD) and fatigue (FAT).[2–4] The prevalence of sleep problems varies depending on, eg, the diagnostic group, gender, and age. In our previous study, we showed that in this sample of patients with psychotic disorders, women had more sleep problems, and that younger age generally, except for EMAs, is associated with more sleep problems. Patients with affective disorders had more insomnia symptoms compared to patients with schizophrenia.[3] Poor sleep is associated with worse prognosis and higher relapse risk and symptom severity in patients with psychotic disorders.[1,5,6] Sleep problems belong to the core symptoms of psychotic disorders,[1] but there have also been findings of a range of both sleep disorders, such as sleep apnea,[7] and lifestyle factors being associated with sleep problems in these patients.[8]

Substance use is known to be associated with sleep problems in the general population.[9,10] Nicotine is associated with shortened sleep duration (short SD), DIS,

EMAs, and increased daytime sleepiness,[11] and the effect seems to be dose-dependent.[12,13] In former smokers, sleep is reminiscent of nonsmokers.[14] Acute administration of high alcohol doses decrease prevalence of DIS, but increases prevalence of EMAs.[15] The decreased prevalence of DIS can diminish in as few as 3 days of continued alcohol use.[16] In chronic use, DIS and EMAs become more common, and total sleep time shortens.[16] Regarding the associations between cannabis use and sleep problems, occasional use does not seem to be associated with sleep problems, in contrast to chronic cannabis use, which is associated with insomnia symptoms and poor sleep quality (poor SQ).[17,18] Benzodiazepines shorten sleep latency (decreased DIS) and increase total SD,[19] but in chronic use, these effects decrease or diminish due to tolerance, and sleep may even improve after discontinuation.[20–22] Many other drugs, including opioids, and psychostimulants such as cocaine and amphetamines, are associated with insomnia symptoms.[10,23,24]

The importance of studying sleep and substance use in patients with psychotic disorders is highlighted by the frequent substance use in this patient group. Estimates of substance use in patients with psychotic disorders vary depending on, eg, the study population (inpatient vs outpatient, cultural factors) and definitions of substance use, as well as whether the substance use is current or lifetime and whether it is self-reported or objectively measured.[25,26] In a register-based study on substance use disorders among patients with schizophrenia in Finland and Sweden, 26% of the Finnish cohort had a substance use disorder diagnosis, with the most common being multiple drug use, followed by alcohol, cannabis, and stimulants.[27] In a large US study including patients with schizophrenia, schizoaffective disorder, and bipolar disorder, use of alcohol, nicotine, cannabis, and other drugs was markedly more common among these patients than in the general population.[28] Substance use has been linked to worse symptoms and outcomes such as poorer cognition,[29,30] higher hospitalization rate,[31] and elevated suicide risk[32] in patients with schizophrenia.

Previous studies on how substance use is associated with sleep problems in patients with psychotic disorders are lacking.[33] One study consisting of primarily cigarette smoking patients with schizophrenia and schizoaffective disorder concluded that the substance use variable (including alcohol, cannabis, and illicit drugs) was associated with the only sleep characteristic assessed, short SD.[34]

The primary objective of this study was to examine how the use of various substances is associated with sleep problems in patients with psychotic disorders in a large nationwide sample from Finland. Our hypothesis was that current smoking and hazardous alcohol use as well as frequent use of illicit drugs during the lifetime are associated with sleep problems, especially insomnia symptoms such as DIS, EMAs, and short SD.

Methods

Study Sample

This study is part of the SUPER research project, which examines psychotic disorders. The SUPER project is incorporated within the international Stanley Global Neuropsychiatric Genomics Initiative. In Finland, the Institute for Molecular Medicine Finland (FIMM), the Finnish Institute of Health and Welfare (THL), and the University of Helsinki oversaw the research project. The project was performed in cooperation with all hospital districts in Finland.

SUPER Sleep Cohort

Patients with schizophrenia spectrum disorders (ICD-10 codes: F20–F29), bipolar disorder, and psychotic depression (International Classification of Diseases (ICD)-10 codes: ICD-10 codes: F30.1, F30.2, F31, F32.3, and F33.3) were invited to participate through psychiatric in- and outpatient units, primary care, housing units, and advertisements in local newspapers from the whole mainland of Finland. In the present study, only patients with schizophrenia, schizoaffective disorder, bipolar disorder, and psychotic depression are included. The diagnoses were retrieved from the Finnish Care Register for Health Care (HILMO). When participants had multiple diagnoses, the diagnoses were considered in the following order of preference: (1) schizophrenia, (2) schizoaffective disorder, (3) bipolar disorder, and (4) psychotic depression. Minors and individuals not able to give informed consent were not recruited into the study. The study protocol has been approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa and by all participating healthcare organizations. The patients were informed about the study by the treating unit, either during a normal appointment, during a hospital stay, or at a nursing home. Research nurses provided the patient with oral and written information on the study and acquired written informed consent, after which the study protocol began.

The total sample size was 10 470 patients. After excluding patients with no registry-based diagnosis or diagnosis other than our 4 diagnostic groups, and patients with an unknown age or older than 80 years (N = 7), 8795 patients remained. Finally, patients who had not answered any sleep question or substance use questions were excluded, leaving 8619 patients. For the study sample flow chart, see Supplementary figure 2.

Demographics

Patients with schizophrenia were the largest diagnostic group in the SUPER sample (demographics in table 1), with 60.2% being men. In the other diagnostic groups, the majority were women. The mean time since first register-based psychosis diagnosis was 8.7 years in 18–40-year-old patients, 20.5 years in 41–60-year-old patients, and 30.2 years in 61–80-year-old patients.

Table 1. Demographics of the Study

	SZ	SZ-A	BD	Ps-DEP
Proportion of sample	*n* = 5597, 64.9%	*n* = 930, 10.8%	*n* = 1586, 18.4%	*n* = 510, 5.9%
Gender (men)	*n* = 3218 57.5%	*n* = 351 37.7%	*n* = 599, 37.8%	*n* = 191, 37.5%
18–40 years	*n* = 1804 32.2%	*n* = 410 44.1%	*n* = 652, 41.1%	*n* = 213, 41.8%
41–60 years	*n* = 2594 46.3%	*n* = 410 44.1%	*n* = 674, 42.5%	*n* = 181, 35.6%
61–80 years	*n* = 1199 21.4%	*n* = 110 11.8%	*n* = 260, 16.4%	*n* = 115, 22.6%
Age, M (SD)	47.8 (13.9)	43.5 (13.6)	45.0 (14.3)	45.1 (17.0)
Low level of education	*n* = 2268, 41.5%	*n* = 223, 24.8%	*n* = 319, 21.3%	*n* = 143, 29.2%
Intermediate level of education	*n* = 544, 50.9%	*n* = 544, 60.5%	*n* = 903, 60.3%	*n* = 290, 59.3%
High level of education	*n* = 418, 7.6%	*n* = 132, 14.7%	*n* = 276, 18.4%	*n* = 56, 11.5%
Married/cohabiting	*n* = 728, 13.0%	*n* = 247, 26.6%	*n* = 612, 38.6%	*n* = 152, 29.9%
Supported living	*n* = 1970, 37.9%	*n* = 136, 15.5%	*n* =120, 7.9%	*n* = 81, 16.6%

Note: SZ, schizophrenia; SZ-A, schizoaffective disorder; BD, bipolar disorder; Ps-DEP, psychotic depression.

Questionnaire

The full questions regarding sleep symptoms and substance use as well as all response categories can be found in the supplement.

Outcome: Sleep Variables. .

The participants filled in a questionnaire that mainly comprised sleep questions from a Finnish population-based study.[35–37] The questions included total sleep duration (TSD), difficulty initiating sleep (DIS)[35], EMAs[35], FAT[36], and SQ[37]. Long SD was defined as sleeping ≥10 h per day, and short SD as sleeping ≤6 h per day. Responses with unreasonable answers to the SD question (TSD < 2 h or ≥ 18 h) were excluded (*N* = 21). DIS, EMAs, and FAT were all defined as having these problems often or nearly always. Poor SQ was defined as having slept rather poorly or poorly.

Substance Use Variables. .

The questionnaire included questions on both current and lifetime substance use. For cigarette smoking, current smoking was our main variable, and this question was from the same Finnish population-based study as the sleep questions.[36] Current smoking was defined as having smoked today or yesterday, while patients having smoked 2 days to 1 month ago were excluded due to probable nicotine withdrawal symptoms.[11,38] Patients with at least one month since their last cigarette were categorized as nonsmokers. Additionally, in our supplemental analyses, lifetime peak cigarette smoking was assessed with the 2 questions from the Heaviness of Smoking Index (HSI).[39] Low HSI was categorized as 1–2 points, moderate as 3–4 points, and high as 5–6 points.[39] In our analyses, we tied the HSI score to the current smoking variable, only considering HSI scores for current smokers.

Alcohol use during the previous 12 months was primarily evaluated with Alcohol Use Disorders Identification Test-Concise (AUDIT-C), a validated screening instrument to identify hazardous alcohol use. This modified version of the 10-item AUDIT includes 3 consumption-focused questions valued from 0 points to 4 points, with a maximum score of 12 points.[40] AUDIT-C was used as a 3-class variable: (1) no alcohol use (0 points); (2) moderate alcohol users, meaning 1–4 points for women and 1–5 points for men; and (3) hazardous alcohol use, meaning 5 points or more for women and 6 points or more for men. These cutoffs were chosen based on the Finnish Guidelines for Alcohol Problems.[41] We also assessed binge drinking separately in a supplemental analysis with AUDIT-3, the third AUDIT-C question. The dichotomous cutoff for binge drinking was having 6 or more drinks monthly or more frequently based on a Finnish study of occupational healthcare patients.[42]

Finally, lifetime use of other substances, ie, illicit drugs, was evaluated with a single question about using any of the substances to get intoxicated, derived from Finnish general population studies,[43] and also used in a previous study on psychotic disorders.[44] When the questionnaire has been used in different studies, the content is updated if new substances of abuse have emerged. In the present study, we focused on the 4 most common of these substances, namely (1) cannabis (marijuana or hashish), (2) benzodiazepines, (3) amphetamines (amphetamine, methamphetamine, MDMA), and (4) opioids (buprenorphine, methadone, heroin, and morphine). Frequent lifetime use or "misuse" of the substance was defined as having used the substance over 50 times to get intoxicated, while occasional users—with rarer use—and patients with no use of the substance were categorized as non-users. The participants were also given the option of responding to "other" with details in free text (*N* = 158). The information retrieved from this was coded into the previously mentioned substance categories if appropriate.

Covariates

The covariates were age, gender, diagnosis, and living status. We categorized the patients into 3 age groups: Young (18–40 years), middle-aged (41–60 years), and elderly (61–80 years).

Living status was retrieved from the interview with the patient:

"Who are you living with now?" The possible answers were "alone," "with spouse," "with spouse and children," "with children and without spouse," "with parents or siblings," "supported housing without night supervision," "supported housing with night supervision," and "other." The answers were categorized into supported housing or living independently. The free text information retrieved from the "other" category (N = 577) was coded based on the same criteria, with the inclusion of long-term hospitalized patients (N = 252) in supported housing and the exclusion of homeless patients (N = 29).

In a post hoc analysis for benzodiazepines, we also took into consideration the prescription use of benzodiazepines. In the study, the names of the medicines were checked on the jar or the prescription if these were available. If no jar or prescription was available, memory information was deemed sufficient. Injections were also recorded. In the post hoc analysis, we excluded patients who had both prescription use of benzodiazepines and use of benzodiazepines to get intoxicated (N = 162), and only patients with use of benzodiazepines to get intoxicated (N = 415) were included. The results were similar, and thus, we include all patients in our analysis.

Statistical Analysis

In bivariate analyses of sleep problems in patients with substance use and in those without substance use, we used chi-square test. In multivariable logistic regression models for sleep problems (DIS, EMAs, FAT, long and short SD, and poor SQ), the explaining variables included diagnostic group, age, gender, living status as confounding factors, and the specific substance in question (alcohol, smoking, cannabis, benzodiazepines, amphetamine, and opioids). Those not using the substance in question or using below threshold levels served as the reference group. Before conducting the final logistic regression analyses, we investigated interactions between age, gender, diagnostic group, and substance use as well as between different substances. However, none of the interactions survived Bonferroni correction for multiple analyses, and therefore, they were dropped from the analyses. Our first logistic regression model included 4 groups of patients: (1) patients with no substance use, (2) patients who used only cigarettes, (3) patients who used only alcohol, and (4) patients who used both cigarettes and alcohol, and excluded patients using other substances. Thereafter, in the second logistic regression model, the rest of the study sample with use of other substances was included. Because the results were similar, we report only the results from the second analysis, including the whole study sample, and the results from the first analyses were included in Supplementary table 2 for regression results).

Results

Prevalence of Substance Use

Cigarettes and alcohol were the most commonly used substances (table 1 for substance use frequencies, Supplementary figure 1 for Venn diagram). The prevalence of hazardous alcohol use during the previous 12 months in this sample was 18.6% (n = 1596), and 46.1% (n = 3783) reported current smoking. There was significant overlap between current alcohol use and cigarette smoking, with 63.6% of hazardous alcohol users also reporting current smoking. Of other forms of lifetime substance use, 10.7% reported using cannabis over 50 times; the corresponding figure for benzodiazepine misuse was 6.7%, for amphetamine misuse 5.3%, and for opioid misuse 3.2%. In all, 44% (n = 3419) of patients were nonusers of the substances, ie, reported no current smoking or hazardous alcohol use, nor did they have any other frequent lifetime substance use. Substance use was more common in men and in younger patients.

Sleep Problems and Substance Use

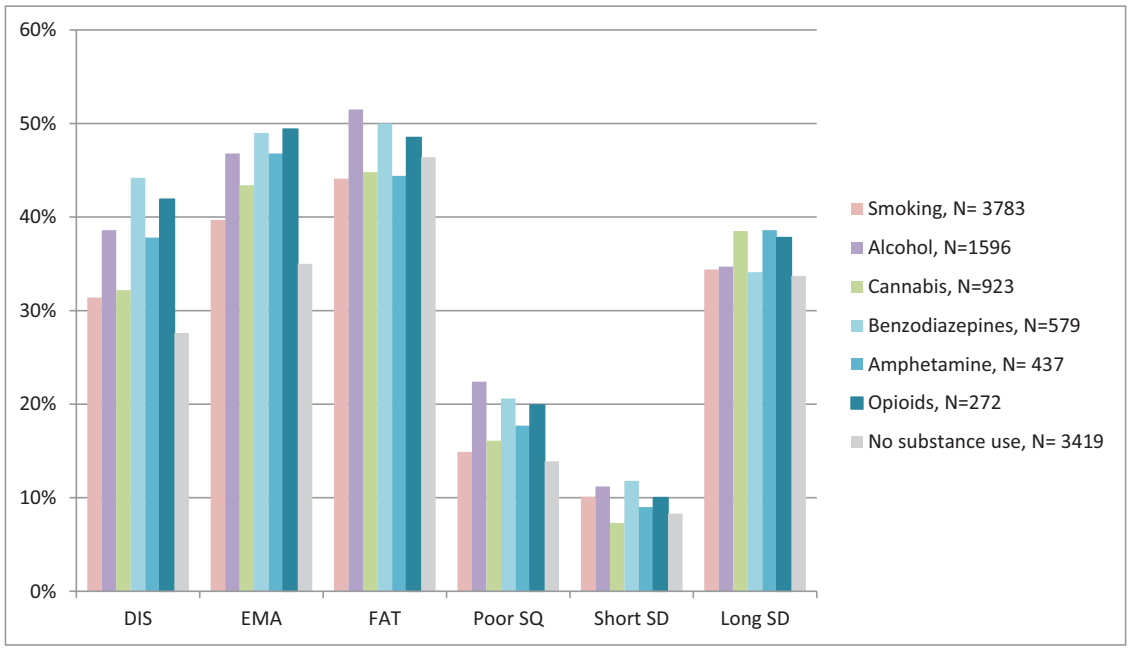
Prevalence of Sleep Problems in Relation to Substance Use. .

As shown in figure 1, the substance use groups overall had more sleep problems than the no substance use group, particularly regarding DIS and EMAs. Patients with hazardous alcohol use and benzodiazepine misuse generally had the highest frequency of sleep problems. For example, EMAs were experienced by 46.8% of patients with hazardous alcohol use and 49.0% of all benzodiazepine misusers relative to 35% of nonusers.

Results From Multivariable Logistic Regression Analyses..

In the multivariable logistic regression models for sleep problems, the confounding factors were age, gender, diagnostic group, and living status. The explaining variables for substance use were hazardous alcohol use (according to AUDIT-C), current smoking, and frequent lifetime use (over 50 times) of cannabis, benzodiazepines, amphetamine, and opioids. Persons with missing values were omitted from the regression analyses. All variables had less than 3% missing values, except for current smoking, which had 5% missing.

Alcohol had the strongest associations with sleep problems in the logistic regression models. In the final model, hazardous alcohol use was associated with more DIS, EMAs, poor SQ, and short SD (table 2). The associations were most apparent with poor SQ (odds ratio [OR] = 1.80, 95% CI: 1.49 to 2.16, P < .001) and EMAs (OR = 1.60, 95% CI: 1.39–1.85, P < .001). Moderate alcohol use was not associated with sleep problems compared with patients who did not use alcohol, but it was associated with less long SD than in patients with no alcohol use. Binge drinking (Supplementary table 2) was



Abbreviations: DIS = Difficulties initiating sleep, EMAs= Early morning awakenings, FAT= Fatigue, Poor SQ= Poor sleep quality, Short SD= Short sleep duration, Long SD= Long sleep duration

Fig. 1. Prevalence of sleep problems according to substance use. Alcohol variable is AUDIT-C, smoking variable is current smoking, and for other substances (cannabis, amphetamines, benzodiazepines, and opioids) they have been used at least 50 times during lifetime.

Table 2. Substance Use in SUPER Sample.

	18–40 M	18–40 F	41–60 M	41–60 F	61–80 M	61–80 F
Alcohol	31.1%	24.5%	20.2%	13.4%	7.5%	3.9%
Smoking	57.9%	43.4%	53.6%	39.2%	43.7%	30.1%
Cannabis	30.8%	9.7%	10.5%	3.2%	1.9%	1.1%
Benzodiazepines	14.7%	5.8%	7.7%	4.0%	2.2%	1.2%
Amphetamines	13.5%	4.6%	5.9%	2.1%	1.1%	0.1%
Opioids	8.5%	3.6%	3.1%	1.2%	0.2%	0.0%

Note: Alcohol variable is hazardous use according to AUDIT-C, smoking variable is current smoking, and for other substances (cannabis, amphetamines, benzodiazepines, and opioids) they have been used to get intoxicated at least 50 times during lifetime.
Note: M, male; F, female.

associated with EMAs (OR = 1.40, 95% CI: 1.14 to 1.72, $P = .002$) and poor SQ (OR = 1.39, 95% CI: 1.06 to 1.83, $P = .02$).

Smoking was associated with shorter SD (OR = 1.28, 95% CI: 1.08 to 1.52, $P = .005$) and less FAT (OR = 0.89, 95% CI: 0.80 to 0.99, $P = .03$) than in those who had not smoked for at least one month (table 2). When we considered the lifetime peak HSI score in patients with current smoking, the picture became more nuanced (Supplementary table 2). Current smoking in combination with high lifetime HSI score (5–6) was associated with DIS (OR = 1.38, 95% CI: 1.06 to 1.78, $P = .015$), EMA (OR = 1.69, 95% CI: 1.33 to 2.15, $P < .001$), poor SQ (OR = 1.50, 95% CI: 1.09 to 2.07, $P = .013$), and short SD (OR = 2.08, 95% CI: 1.44 to 3.01, $P < .001$). On the other hand, smoking with low HSI score was associated with less sleep problems, including EMAs, poor SQ, and FAT, than no cigarette use.

Frequent benzodiazepine misuse during the lifetime was associated with more DIS, EMA, FAT, short SD, and poor SQ, and less long SD. The association was strongest with DIS (OR = 2.00, 95% CI: 1.55 to 2.48, $P < .001$). By contrast, using cannabis, amphetamine, and opioids more than 50 times during the lifetime was not associated with any of the sleep problem categories being examined.

Regarding covariates, patients with schizoaffective disorder, bipolar disorder, and psychotic depression had more sleep problems than patients with schizophrenia, excluding long SD, which was most prevalent among patients with schizophrenia. Women had more sleep problems than men, and young patients had more long SD and FAT than older patients, but less DIS, EMAs, and

Table 3. Results From Logistic Regression With Difficulties Initiating Sleep, Early Morning Awakenings, Fatigue, Sleep Quality, and Long And Short Sleep Duration

Difficulties Initiating Sleep	OR	CI	*P*	Early Morning Awakenings	OR	CI	*P*	Fatigue	OR	CI	*P*
Gender[a]	1.21	1.08 to 1.34	.001		1.28	1.16 to 1.41	<.001		1.49	1.35 to 1.64	<.001
Diagnosis[b]			<.001				.002				<.001
SZ-A	1.36	1.15 to 1.61	<.001		1.13	0.97 to 1.33	.130		1.16	0.99 to 1.35	.064
BPD	2.07	1.81 to 2.36	<.001		1.26	1.11 to 1.44	<.001		1.51	1.32 to 1.71	<.001
Ps-DEP	2.28	1.85 to 2.80	<.001		1.25	1.02 to 1.54	.033		1.53	1.24 to 1.87	<.001
Age[c]			<.001				<.001				<.001
41–60 years	1.28	1.14 to 1.45	<.001		1.54	1.38 to 1.73	<.001		0.70	0.63 to .078	<.001
61–80 years	1.48	1.27 to 1.72	<.001		1.69	1.46 to 1.95	<.001		0.42	0.36 to 0.49	<.001
Living status[d]	0.88	0.77 to 1.00	.050		0.95	0.85 to 1.07	.427		0.98	0.87 to 1.10	.710
Alcohol use[e]			<.001				<.001				.253
Moderate use	0.94	0.83 to 1.06	.302		0.96	0.85 to 1.07	.446		1.04	0.93 to 1.17	.460
Hazardous use	1.42	1.22 to 1.65	<.001		1.60	1.39 to 1.85	<.001		1.13	0.98 to 1.30	.098
Smoking[f]	1.10	0.98 to 1.23	.093		1.06	0.96 to 1.18	.247		0.89	0.80 to 0.99	.025
Cannabis[g]	0.85	0.68 to 1.07	.160		1.22	0.99 to 1.50	.061		0.83	0.68 to 1.02	.079
Benzodiazepines[h]	2.00	1.56 to 2.57	<.001		1.59	1.25 to 2.02	<.001		1.47	1.15 to 1.87	.002
Amphetamines[i]	1.02	0.71 to 1.45	.934		1.02	0.73 to 1.43	.900		0.93	0.67 to 1.30	.689
Opioids[j]	1.22	0.81 to 1.84	.338		1.15	0.78 to 1.70	.488		0.95	0.64 to 1.41	.813
Long Sleep Duration				**Short Sleep Duration**				**Sleep Quality**			
Gender	1.24	1.12 to 1.37	<.001		0.93	0.78 to 1.09	.360		1.37	1.19 to 1.57	<.001
Diagnosis			<.001				<.001				<.001
SZ-A	0.86	0.73 to 1.01	.064		1.32	1.01 to 1.72	.040		1.44	1.17 to 1.77	.001
BPD	0.64	0.56 to 0.74	<.001		1.52	1.23 to 1.87	<.001		2.10	1.79 to 2.48	<.001
Ps-DEP	0.52	0.41 to 0.66	<.001		1.96	1.45 to 2.65	<.001		2.29	1.79 to 2.92	<.001
Age			<.001				<.001				.237
41–60 years	0.61	0.55 to 0.69	<.001		2.06	1.66 to 2.55	<.001		1.12	0.96 to 1.30	.152
61–80 years	0.37	0.32 to 0.43	<.001		3.42	2.67 to 4.37	<.001		0.90	0.81 to 1.21	.899
Living status	1.32	1.17 to 1.48	<.001		0.85	0.70 to 1.05	.126		0.79	0.66 to 0.95	.011
Alcohol			.020				.007				<.001
Moderate use	0.84	0.75 to 0.95	.005		0.89	0.74 to 1.09	.265		1.11	.95 to 1.30	.193
Risk use	0.90	0.78 to .1.05	.185		1.30	1.03 to 1.64	.026		1.80	1.49 to 2.16	<.001
Smoking	0.97	0.87 to 1.08	.567		1.28	1.08 to 1.52	.005		0.91	0.79.1.05	.181
Cannabis	1.14	0.93 to 1.41	.212		0.72	0.48 to 1.06	.098		0.99	0.75 to 1.31	.924
Benzodiazepines	0.76	0.59 to 0.99	.040		1.60	1.11 to 2.30	.012		1.42	1.05 to 1.93	.023
Amphetamines	0.83	0.68 to 1.36	.829		1.14	0.64 to 2.02	.665		1.11	0.72 to 1.72	.634
Opioids	0.90	0.60 to 1.36	.613		1.50	0.80 to 2.79	.204		1.24	0.76 to 2.04	.385

Note: Alcohol variable is AUDIT-C, smoking variable is current smoking, and for other substances (cannabis, amphetamines, benzodiazepines, and opioids) they have been used to get intoxicated at least 50 times during lifetime.
Note: SZ-A, schizoaffective disorder; BD, bipolar disorder; Ps-DEP, psychotic depression.
Note: Information follows.
[a]Reference group: Men.
[b]Reference group: Schizophrenia.
[c]Reference group: 18–40-year-old patients.
[d]Reference group: people who live in supported housing (as opposed to living independently).
[e]Reference group: Patients with no alcohol use.
[f]Reference group: Patients with no smoking in at least 1 month.
[g,h,i,j]Reference group: Patients who have not at all or only occasionally (under 50 times) used the substance in question during lifetime.

short SD. Patients in supported housing had more long SD and poor SQ than those living independently (table 3).

Discussion

General Results

This study aimed to examine associations between sleep problems and substance use in a large sample of patients with psychotic disorders. To the best of our knowledge, no previous large-scale study has been conducted on this subject. Generally, the use of substances was associated with higher prevalence of sleep problems, including short SD, poor SQ, EMAs, FAT, and DIS.

Current hazardous, but not moderate level, alcohol use was associated with a range of sleep problems, consistent with previous research in the general population.[16] The strongest associations were with poor SQ and EMAs, with 22.4% of hazardous alcohol users having poor SQ, compared to 13.9% of those with no substance use. Binge drinking was also associated with poor SQ and EMAs. Our results emphasize the importance of screening hazardous alcohol use among psychosis patients with sleep problems. Studies examining the neurobiology of alcohol use have confirmed the strong link between sleep and alcohol, with GABA-receptor agonism in acute intoxication promoting less DIS. The downregulation of the same GABA receptors in chronic use is one of the central mechanisms for later sleep problems.[45,46]

Current smoking was associated with short SD, and less FAT. Of current smokers, 10.1 % had short SD, compared to 8.3 % of those with no substance use. In our additional analysis, we coupled current smoking with peak lifetime cigarette smoking levels (HSI)—which could be current or past. In this analysis, heavy smoking—current or history of such—was broadly associated with more sleep problems, while current light cigarette smoking was associated with less sleep problems compared to patients with no current smoking. Cigarette dose dependency for associations with sleep problems is in line with earlier research in adults with no psychiatric comorbidities.[12,13] To the best of our knowledge, there are no previous studies reporting less FAT in current smokers than in nonsmokers or reporting that light smoking is associated with less sleep problems. In this context, the pharmacological interactions between nicotine and antipsychotic medications, such as olanzapine and clozapine, are of interest, as nicotine increases the clearance of these drugs. Thus, smoking may alleviate adverse effects like FAT.[47] One possible contributor to the findings of less FAT and more short SD could be the innate stimulant effects of nicotine through nicotinic receptor agonism.[48]

Of the other substances, frequent benzodiazepine misuse during a lifetime was associated with sleep problems. However, it is important to note that because of the cross-sectional setup here, causality cannot be determined. From previous studies, long-term use of benzodiazepines is known to be associated with increasing tolerance[20] and changes in sleep architecture.[49] Anxiety and other affective symptoms driving recreational benzodiazepine use[50] while simultaneously impairing sleep, is a possible confounder that was not fully accounted for. We did conduct a post hoc analysis excluding patients with benzodiazepine prescriptions, as these patients can be seen as having probable clinical reasons for their benzodiazepine use, with no significant results changing.

The differences in sleep problems between the diagnostic groups followed the same pattern as in our previous study,[3] where substance use was not considered. Insomnia symptoms—meaning DIS, EMAs, and short SD—as well as FAT and poor SQ were generally more common in patients with schizoaffective disorder, bipolar disorder, or psychotic depression, while long SD was most common in patients with schizophrenia. The differences between affective psychotic disorders and schizophrenia were generally of the same size as those for substance use, meaning alcohol, cigarette smoking, and benzodiazepines vs nonuse. Taking substance use into account did not change the results regarding age and gender.

Strengths and Limitations

One of the strengths of this study is the large, nationwide sample, which enabled separating the patients into diagnostic groups and the substance use into various substance use groups, instead of merging these together. The sleep problems were also assessed comprehensively. However, even with a sample size as large as in this study, history of use (especially sole use) of some of the substances, such as cannabis, amphetamines, and opioids, was quite rare. This limited statistical power, and the absence of knowledge regarding current use, might explain the lack of associations between these substances and sleep problems, which in previous studies have been associated with sleep problems.[10,17,23,24,51,52]

The following limitations should be considered when interpreting the results of this study. First, current substance abuse was only queried in the context of alcohol use and smoking and not for other substances. Regarding other substances, we only had information on use never, occasionally, or over 50 times during the lifetime. Current substance use is expected to have a larger effect on sleep than previous substance use. In future studies, more specific information on current substance use and withdrawal symptoms as well as on duration of use and use patterns should be sought. Second, information on sleep and substance use was based on self-reports. Third, no medications used by patients, apart from benzodiazepine, were considered in the post hoc analysis. These factors should be addressed in future studies investigating sleep in psychotic disorders.

Conclusions

To the best of our knowledge, this is the first large-scale study reporting associations between substance use and sleep problems among persons with psychotic disorders. According to our findings, current hazardous alcohol use and cigarette smoking as well as lifetime benzodiazepine use are associated with various sleep problems, including difficulties falling asleep, EMAs, poor SQ, and short SD. These findings—especially considering how common both substance use, and sleep problems are in these patients—highlight the need to screen substance use in patients with psychotic disorders who have sleep problems, and to educate the patients about possible links between substance use and sleep problems.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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