Parasomnia Among Psychiatric Outpatients: A Clinical, Epidemiologic, Cross-Sectional Study

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Objective: Epidemiologic studies from general population and clinical case series suggest association of parasomnias with mental illnesses and psychotropic medications. This cross-sectional study aimed at determining the prevalence rate of sleepwalking, sleep-related eating disorder (SRED), rapid eye movement sleep behavior–like disorder (RSBD-like disorder), and sleep-related injury (SRI) and their associated factors in an adult psychiatric outpatient clinic.

Method: Subjects aged 18 to 65 years who were attending an outpatient clinic in Hong Kong from May 2006 through June 2006 were included in this cross-sectional study. A 3-phase design was employed, including a structured questionnaire on parasomnias, followed by clinical interviews of both questionnaire-positive and -negative groups, and polysomnography for subjects having active parasomnias in recent 1 year. In addition, the principal psychiatric diagnoses, medical illnesses, and detailed drug history over recent 1 year were retrieved from the computerized records.

Results: Twelve hundred thirty-five subjects completed the phase 1 interview. The estimated prevalence of the lifetime diagnoses of sleepwalking, SRED, SRI, sleep violence, and RSBD-like disorder were 8.5%, 4.0%, 21.0%, 3.6%, and 5.8%, respectively, while the 1-year prevalence of these conditions were 2.9%, 2.4%, 8.8%, 2.5%, and 3.8%, respectively. These conditions were associated with depression and a constellation of sleep disturbances. Specific combinations of psychotropics were found to pose risk in particular parasomnias: sedative antidepressants and nonbenzodiazapine hypnotics in sleepwalking, regular zolpidem and antidepressants in SRED, and selective serotonin reuptake inhibitors in RSBD-like disorder.

Conclusions: Sleepwalking, SRED, RSBD-like disorder, and SRI were common and underrecognized among the psychiatric population in this study. Their occurrences were likely contributed by interacting effect of mental illnesses, sleep disturbances, and specific psychotropic medications. Further prospective study is warranted for clarification of the etiology and clinical management of these potentially dangerous and "hidden" parasomnias.

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Parasomnia refers to a group of sleep disorders characterized by abnormal sleep-related movements, perceptions, dreaming, and autonomic arousals that occur at different sleep stages. Parasomnia could contribute to sleep disruptions, mental distress, and potential serious sleep injuries to both subjects and their bed partners. In the past, parasomnia was mainly regarded as a manifestation of underlying psychiatric problems. For example, sleepwalking was viewed as a dissociative disorder and dream enactment of repressed traumatic experiences.[1] With the advance and development of sleep medicine, the old concept changed and sleepwalking is now regarded as an independent disorder with a complex etiology of genetic, neurophysiologic, and psychopathologic basis.[2] However, epidemiologic studies among the general population suggested there were still correlations between parasomnia and psychiatric illnesses, such as sleepwalking and affective disorders[3,4] and sleep-related eating disorder (SRED) and eating disorders.[5] The underlying mechanism for how these illnesses interact remains obscure.

In parallel to the epidemiologic studies, there has been an increasing number of case reports of psychotropic-related parasomnias, including nonbenzodiazepine hypnotics, antidepressants, and combinations of psychotropics.[6–19] Both the U.S. Food and Drug Administration and Therapeutic Goods Administration of Australia

TAKE-HOME POINTS

- Parasomnias such as sleepwalking, sleep-related eating disorder, and rapid eye movement sleep behavior–like disorder, are frequently overlooked and underdiagnosed in psychiatric settings. They could result in serious sleep-related injuries to both subjects and their bed partners as well as other adverse health consequences.
- These parasomnias are associated with a constellation of risk factors, including depression, comorbid sleep disturbances, and specific psychotropic medications.
- Clinicians should have heightened alertness for these "hidden" parasomnias.

have recently issued warnings[20,21] regarding psychotropic-related parasomnia, including benzodiazepine-related sleepwalking and nonbenzodiazepine hypnotic–related SRED.

Given the background of the associations among parasomnia, psychiatric illnesses, and medications, epidemiologic study of parasomnia in psychiatric populations can help in determining the magnitude of the problem and shed light on the associated factors and possible etiologies of these parasomnias. In this study, we aimed at looking for the prevalence rate and associated factors of parasomnias that are characterized by dramatic movement with potentially serious consequences, which include sleepwalking, SRED, and rapid eye movement (REM) sleep behavior–like disorder (RSBD-like disorder).

METHOD

Inclusion and Exclusion Criteria

This was a cross-sectional study in a regional public psychiatric outpatient clinic that served 8.9% (0.6 million) of the total population in Hong Kong. It was approved by the institutional ethics committee, and written informed consent was obtained from the recruited subjects. The study design consisted of 3 phases. Adult subjects aged 18 to 65 years attending the clinic within a 4-week period from May 2006 to June 2006 were targeted for the study. They were excluded if they met any of the following criteria: (1) mental retardation or dementia, (2) non-Chinese, (3) hearing or speech impairment, (4) unstable mental condition that hampered the subjects in giving a valid consent, and (5) sleep clinic attendees.

Procedures, Assessment, and Instruments

Phase 1. Face-to-face interviews were conducted by trained interviewers with the consented subjects and their relatives if they were available. The structured questionnaire consisted of questions about demographics and sleep habits and problems. As self-reported, brief questions of parasomnia were used as a screening tool, familiarity of a condition could enhance the accuracy of the questionnaires.[22] Compared with RSBD, sleep-related injury (SRI), one of the diagnostic criteria for RSBD, is a broader and more understandable lay phenomenon and is more readily assessed by self-report. Hence, direct questions regarding SRI rather than RSBD were applied in the phase 1 questionnaire.

Screening questions for sleepwalking, SRED, and SRI were as follows: (1) Have you ever had any sleepwalking (sitting up, leaving bed, or carrying out acts during sleep that you were not in full awareness of and you had little recall on waking up)? (2) Have you ever consumed food or drinks during sleep that you were not in full awareness of during the episode? (3) Have you ever fallen from bed or inflicted injuries to yourself or others during your sleep? Each question was followed by further details on frequency of the episodes and whether the subjects had any episode in recent 1 year (Questionnaire [in Chinese] is available on request [Y.W.].).

Relevant clinical information from the clinical management system was reviewed for the subjects' principal psychiatric diagnoses, medical illnesses, and drug history. The clinical management system is an integrated computerized clinical workstation that was implemented in 1995 in all the public hospitals of Hong Kong. A list of psychotropic medication, including types and duration, that the subjects were taking at the time of interview and during the past 1 year was recorded.

Phase 2. Those who responded positively to either one of the questions about sleepwalking, SRED, and SRI were invited to phase 2 clinical interviews. Family members and bed partners were invited for collateral information with subjects' consent. Details of the events and sleep history were explored and recorded. Diagnosis of sleep problems was defined according to criteria established in the *International Classification of Sleep Disorders: Diagnostic and Coding Manual, 2nd Edition*,[23] and the severity of SRI and sleep violence (moderate to severe degree of SRI) was defined in Table 1.

A random sample of the questionnaire-negative group (13.5%) was interviewed for validation and calculation of estimated prevalence.

Phase 3. Subjects having active SRED or RSBD-like disorder in recent 1 year were invited for 2 consecutive

Table 1. Definitions of Sleepwalking, Sleep-Related Eating Disorder, Rapid Eye Movement Sleep Behavior–Like Disorder, and Sleep-Related Injury[a]

A. Sleepwalking
1. Ambulation occurs during sleep
2. An altered state of consciousness or impaired judgment during ambulation is demonstrated by at least 1 of the following:
i. Difficulty in arousing the person
ii. Mental confusion when awakened from an episode
iii. Amnesia (complete or partial) for the episode
iv. Routine behaviors that occur at inappropriate times
v. Inappropriate or nonsensical behaviors
vi. Dangerous or potentially dangerous behavior
B. Sleep-related eating disorder
1. Recurrent episodes of involuntary eating and drinking occur during the main sleep period
2. One or more of the following must be present with the recurrent episodes of involuntary eating and drinking:
i. Consumption of peculiar forms or combinations of food or inedible or toxic substances
ii. Insomnia related to sleep disruption from related episodes of eating, with a complaint of nonrestorative sleep, daytime fatigue, or somnolence
iii. Sleep-related injury
iv. Dangerous behavior performed while in pursuit of food or cooking food
v. Morning anorexia
vi. Adverse health consequences from recurrent binge eating of high-caloric foods
3. An altered state of consciousness usually demonstrated during the episodes
C. Rapid eye movement sleep behavior–like disorder[b]
1. A complaint of violent or injurious behavior during sleep
2. Limb or body movement associated with dream mentation
3. At least 1 of the following:
i. Harmful or potentially harmful sleep behavior
ii. Dreams appear to be "acted out"
iii. Sleep behaviors disrupt sleep continuity
D. Sleep-related injury
1. Mild degree of injury: bruising or superficial injuries requiring no treatment
2. Moderate degree of injury: laceration or assaulting others that requires medical treatment
3. Severe degree of injury: serious injury that requires hospitalization or dangerous or life-threatening assault to bed partners
E. Sleep violence is defined as those sustaining moderate and severe degree of injury

[a]The diagnostic criteria were adapted with permission from *International Classification of Sleep Disorders*, 2nd Edition (ICSD-2).[23]
[b]This definition was modified from ICSD-2 rapid eye movement sleep behavior disorder (RSBD) criteria, which consisted of only the clinical features but not the polysomnographic criteria of RSBD.

nocturnal polysomnographic (PSG) studies for documentation of PSG features of the disorders. Sleepwalking was not included in PSG study because of its episodic nature, and the diagnosis was mostly based on clinical history. Subjects were instructed to continue their medications and sleep habits as usual. The PSG study was simultaneously videotaped for any sleep-related movement. If the subjects were found to have an apnea-hypopnea index greater than 5 during first night, continuous positive airway pressure treatment was on the second night. Polysomnographic monitoring included electrooculogram, electroencephalogram (EEG), electromyogram (monitoring over chin and bilateral anterior tibialis muscles), electrocardiogram, nasal-oral airflow, respiratory movements, arterial oxygen saturation, and body position. The PSG study was scored according to standard criteria for sleep staging, respiratory events, limb movements, and arousal,[23] but the scorers were not blind to the clinical diagnosis.

Statistical Analysis

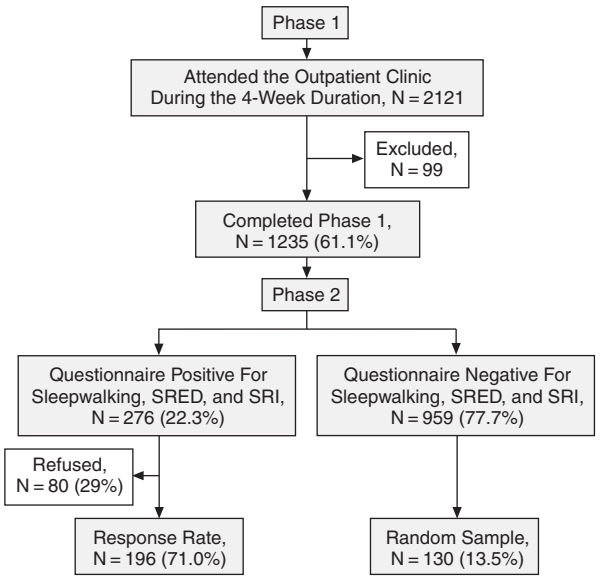
Data were weighted for the sampling procedure for the estimated prevalence of sleepwalking, SRED, and SRI.[24] Univariate analysis of nonparametric data was performed using χ^2 statistics. Fisher exact test was applied when N values were smaller than 5. Student t test was used for continuous data. Predictive variables for sleepwalking, SRED, and RSBD-like disorders were determined by logistic regression in separate models. The cutoff point of the selected variables for logistic regression was fixed at $p < .10$. Statistical Package for the Social Sciences, version 14.0 (SPSS Inc., Chicago, Ill.) was used for data analysis.

RESULTS

Demographics and Response Rate of the Subjects

During the 4-week period, 2121 psychiatric outpatients attended the clinic. According to the criteria, 99 subjects were excluded. The target sample consisted of 2022 subjects, and 61.1% (N = 1235) of the subjects (recruited group) completed the phase 1 interview (Figure 1). After comparing these subjects with the refusal group (N = 787), we found no significant difference in age. However, the recruited subjects compared with the refusal groups were composed of slightly more women (68.1% vs. 60.7%, $p < .01$) and more depressive (34.1% vs. 28.0%, $p < .01$) and anxiety spectrum disorders (14.7%

Figure 1. Logistic Flowchart and Response Rate of Phase 1 and Phase 2



Abbreviations: SRED = sleep-related eating disorder, SRI = sleep-related injury.

vs. 11.1%, $p < .05$) but fewer psychotic spectrum disorders (33.4% vs. 38.2%, $p < .05$). The demographic features of the recruited subjects are shown in Table 2. One third of the recruited subjects were diagnosed according to criteria in *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research*[25] with depressive spectrum disorder, followed by psychotic spectrum disorder, anxiety spectrum disorder, and bipolar affective disorder. A minority were given diagnoses of substance abuse (1.9%) and eating disorder (1%). About 3% of the subjects had no definite psychiatric diagnosis.

In the phase 2 study, 276 subjects (22.3%) responded positively to the questions about sleepwalking, SRED, and SRI (Figure 1). Among these subjects, 71% (N = 196) underwent the phase 2 clinical interview. There were no significant differences between the interviewed and refusal groups over gender, age, psychiatric diagnoses, and medical illness.

Regarding the questionnaire-negative group, 130 (13.5%) of 959 subjects were selected randomly for the phase 2 interview. There were no significant differences over living status, medical illnesses, and diagnoses of psychotic spectrum disorder, bipolar affective disorder, and anxiety spectrum disorder. However, the interviewed group compared with the noninterviewed group had more women (75.4% vs. 66.1%, $p < .05$), older age (mean ± SD: 45.6 ± 10.0 vs. 42.3 ± 11.6 years, $p < .05$), and higher prevalence of depressive spectrum disorder (37.7% vs. 28.3%, $p < .05$).

Table 2. Demographic and Clinical Characteristics of Recruited Subjects (N = 1235) in the Phase 1 Interview[a]

Variable	Value
Gender (male:female)	31.9:68.1
Age, mean ± SD, y	42.4 ± 11.3
Body mass index, mean ± SD	23.8 ± 4.3
Medical illness	20.2
Psychotic spectrum disorder[b]	33.4
Bipolar affective disorder[c]	11.7
Depressive spectrum disorder[d]	34.1
Anxiety spectrum disorder[e]	14.7
Antidepressant	53.9
SSRI	35.6
SNRI	5.4
NaSSA	3.1
Tricyclic antidepressant	10.4
Nonbenzodiazepine hypnotic	17.0
Zolpidem	7.2
Zopiclone	9.9
Benzodiazepine	36.0
Antipsychotic	52.4
Mood stabilizer	18.3
Polypharmacy (≥ 2 psychotropics)	71.4

[a]Values are presented as percents except where otherwise indicated.
[b]Psychotic spectrum disorders include schizophrenia, schizoaffective disorder, and delusional disorder.
[c]Bipolar affective disorders include bipolar disorder types I and II.
[d]Depressive spectrum disorders include depression (single and recurrent) and dysthymia.
[e]Anxiety spectrum disorders include panic disorder, agoraphobia, generalized anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and adjustment disorder.
Abbreviations: NaSSA = noradrenergic and specific serotonergic antidepressant, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

Psychometric Properties of the Questionnaire

Although the questionnaire had apparent face validity, the psychometric properties were further determined by using a clinical interview as the confirmatory criteria of the parasomnia. The sensitivity of individual questions on sleepwalking, SRED, and SRI were 0.68, 0.78, and 0.86, respectively, and specificity of questions on sleepwalking, SRED, and SRI were 0.95, 0.96, and 0.84, respectively. The positive predictive value (PPV) of sleepwalking, SRED, and SRI were 0.78, 0.64, and 0.79, respectively. The negative predictive value (NPV) of sleepwalking, SRED, and SRI were 0.92, 0.98, and 0.90, respectively. The sensitivity, specificity, PPV, and NPV of the overall questionnaire were 0.92, 0.83, 0.88, and 0.88, respectively. The psychometric properties of the individual and overall questions were satisfactory and comparable.

Prevalence Estimates

The estimated lifetime prevalence rates for subjects with sleepwalking, SRED, SRI, sleep violence, and RSBD-like disorder were 8.5%, 4.0%, 21.0%, 3.6%, and 5.8%, respectively. The estimated 1-year prevalence rates for those with sleepwalking, SRED, SRI, sleep violence, and RSBD-like disorder were 2.9%, 2.4%, 8.8%, 2.5%, and 3.8%, respectively.

Table 3. Demographics, Sleep Disturbances, Mental Illness, and Psychotropic Use Among Groups With Parasomnia and Nonparasomnia (movement related)[a]

Variable	Nonparasomnia (movement related) (N = 944)[b]	Sleepwalking (N = 29)[c]	SRED (N = 22)[c]	RSBD-Like Disorder (N = 30)[c]
Female gender	67.6	72.4	81.8	56.7
Age, mean ± SD, y	42.7 ± 11.5	43.3 ± 10.6	41.5 ± 10.9	40.2 ± 9.7
Body mass index, mean ± SD	23.7 ± 4.4	24.7 ± 4.6	24.6 ± 4.5	23.7 ± 3.7
Medical illness	18.8	41.4*	27.3	23.3
Insomnia, > 3/wk	32.5	58.6*	77.3**	60.0*
Snoring	19.8	41.4*	40.9*	40.0*
Nightmare, > 1/mo	16.8	55.2**	50.0*	60.0**
Frequent sleeptalking	4.3	13.8*	4.5	10.0
Frequent bruxism	5.1	10.3	9.1	26.7**
Night terror	5.1	17.2*	18.2*	23.3*
Sleep-related hallucination	8.1	24.1*	27.3*	10.0
Sleep paralysis, > 1/mo	3.4	13.8*	13.6*	20.0*
Depressive spectrum disorder	29.6	58.6*	59.1*	63.3*
Bipolar affective disorder	12.4	10.3	9.1	6.7
Psychotic spectrum disorder	35.6	20.7	9.1*	6.7*
Anxiety spectrum disorder	15.3	6.9	13.6	20.0
Antidepressant	49.3	82.8*	95.5**	86.7**
SSRI	32.4	51.7	72.7**	70.0**
SNRI	5.2	13.8	13.6	10.0
NaSSA	2.1	6.9	4.5	10.0*
Sedative antidepressant[d]	12.7	34.5*	31.8*	20.0
Nonbenzodiazepine hypnotic	14.3	62.1**	72.7**	26.7
Zolpidem	5.4	44.8**	63.6**	10.0
Zopiclone	8.9	24.1*	18.2	16.7
Benzodiazepine	35.6	44.8	45.5	43.3
Antipsychotic	56.0	44.8	27.3*	46.7
Mood stabilizer	19.2	27.6	27.3	16.7

[a]Values are presented as percents except where otherwise indicated.
[b]Subjects without sleepwalking, sleep-related eating disorder, or RSBD-like disorder. This group of subjects comprised the questionnaire-negative group in phase 1 by excluding the false-negative subjects.
[c]Having experienced in the recent 1 year as confirmed by the phase 2 clinical interview.
[d]Sedative antidepressants include tricyclic antidepressants, trazodone, and mianserin.
*p < .05., **p < .001. Nonparasomnia is the reference group.
Abbreviations: NaSSA = noradrenergic and specific serotonergic antidepressant, RSBD-like disorder = rapid eye movement sleep behavior–like disorder, SNRI = serotonin-norepinephrine reuptake inhibitor, SRED = sleep-related eating disorder, SRM = sleep-related movement, SSRI = selective serotonin reuptake inhibitor.

Type, Severity, and Diagnosis of Sleep-Related Injury

Among subjects reporting SRI who underwent the phase 2 interview (N = 133), the majority (82.7%) reported a mild degree of injury to themselves and/or bed partners, 14.3% had sustained a moderate degree of injury such as laceration or had assaulted bed partners by kicking and hitting that required medical treatment, and 3.0% had sustained a severe degree of injury or had serious assault on bed partners such as strangulation (Table 1). There were no gender differences across the different degrees of injury. Those having sleep violence were more likely to have a psychiatric diagnosis of depressive spectrum disorder (sleep violence, 78.3%; mild sleep injury, 43.6%; non-SRI, 32.2%; p < .001) but less likely to have a psychotic spectrum disorder (sleep violence, 4.3%; mild injury, 22.7%; non-SRI, 35.0%; p < .001). Subjects with SRED were found to have committed dangerous acts, including cooking, burning pot (without water) on stove, and consuming frozen food under impaired consciousness.

Regarding the causes of SRI, 73% (N = 51/70) of subjects with SRI were given a diagnosis of parasomnia as the major cause of the injuries. The other causes of injury included confusion (4.3%), sleep apnea (2.9%), environmental factors (such as crowded beds, nonsleep-related condition, or injuries inflicted by bed partners) (8.6%), and undetermined causes (11.4%). Among different types of parasomnia (N = 51), REM-related parasomnia (including RSBD-like disorder, nightmares, and mixed REM and nonrapid eye movement [NREM] parasomnia) accounted for the majority (66.6%, N = 34), followed by sleepwalking (13.6%, N = 7), SRED (7.8%, N = 4), periodic leg movement syndrome (10.0%, N = 5), and sleep-related hallucination (2.0%, N = 1).

Demographics and Sleep Disturbance Among Subjects With Parasomnia

Gender, age, and body mass index were comparable between subjects with parasomnia and those with nonparasomnia (movement related) (Table 3). Those having sleepwalking had more medical illness. Sleep disturbances, including insomnia, snoring, recurrent nightmares, night terror, and sleep paralysis, were more

common in all 3 groups with parasomnia. Bruxism was more commonly reported by the RSBD-like disorder group. A greater proportion of sleepwalking and SRED subjects reported recurrent sleep-related hallucinations.

Association of Parasomnias With Mental Illness and Psychotropic Medications

Subjects with depressive spectrum disorder reported a significantly higher percentage of sleepwalking, SRED, and RSBD-like disorder than the subjects with nonparasomnia (movement related). In opposite, subjects having psychotic spectrum disorders had less report of SRED and RSBD-like disorder. Bipolar affective disorder and anxiety spectrum disorder had no significant association with these parasomnias (Table 3).

Subjects taking antidepressants reported more sleepwalking, SRED, and RSBD-like disorder but the association varied with different types of antidepressants. Selective serotonin reuptake inhibitors were particularly associated with SRED and RSBD-like disorder, while sedative antidepressants were more prevalent in sleepwalking and SRED subjects. Nonbenzodiazepine hypnotics were also commonly used in subjects with active sleepwalking and SRED. However, only zolpidem, but not zopiclone, was significantly associated with SRED. One of 7 subjects taking zolpidem developed SRED. Those at risk were more likely taking regular dosage (92% in SRED vs. 54% in non-SRED group, $p < .05$) rather than taking it on an as-necessary basis. Polypharmacy was also more common in both sleepwalking and SRED groups. Among all the psychotropics, antipsychotic medication had negative association with SRED. The remaining classes of psychotropics, including benzodiazepine and mood stabilizers, did not have significant association with the parasomnias (Table 3).

Logistic Regression

Variables found to be significant in univariate analysis were entered into 3 separate stepwise logistic regression models. For sleepwalking, factors including medical illnesses (OR = 3.2, 95% CI = 1.4 to 7.3, $p < .05$), nightmares (OR = 3.9, 95% CI = 1.8 to 8.5, $p < .05$), sedative antidepressants (OR = 2.4, 95% CI = 1.1 to 5.8, $p < .05$), and nonbenzodiazepine hypnotics (OR = 6.8, 95% CI = 3.0 to 15.1, $p < .001$) were associated with higher risk of having active sleepwalking. The following variables were found to be independently related to SRED in logistic regression: snoring (OR = 3.5, 95% CI = 1.3 to 9.8, $p < .05$), sleep-related hallucination (OR = 4.0, 95% CI = 1.3 to 12.7, $p < .05$), nightmares (OR = 3.1, 95% CI = 1.2 to 8.2, $p < .05$), SSRIs (OR = 5.1, 95% CI = 1.6 to 16.6, $p < .05$), sedative antidepressants (OR = 4.7, 95% CI = 1.4 to 15.9, $p < .05$), and the use of zolpidem (OR = 22.1, 95% CI = 8.2 to 59.8, $p < .001$). Subjects with nightmares (OR = 4.3, 95% CI = 1.9 to 8.6, $p < .05$), bruxism (OR = 4.5, 95% CI = 1.8 to 11.3, $p < .05$), sleep paralysis (OR = 3.1, 95% CI = 1.1 to 9.0, $p < .05$), and those taking SSRIs (OR = 3.7, 95% CI = 1.6 to 8.7, $p < .05$) had increased risk of having active RSBD-like disorder. Among those taking SSRIs, 5% were found to report RSBD-like symptoms.

Polysomnographic Result

In our study, 3 (13.6%) of 22 SRED subjects and 13 (43.3%) of 30 subjects with RSBD-like disorder completed the phase 3 PSG study. There were no significant differences over age, gender, psychiatric diagnoses, and degree of sleep injury between the study and nonstudy groups. Among the 3 active SRED subjects, no automatism or eating behavior was demonstrated during PSG study, probably due to the episodic nature of the disorder. They had no EEG abnormalities, and 1 was found to have a moderate degree of obstructive sleep apnea syndrome (OSAS).

Regarding the 13 subjects with RSBD-like disorder, 11 of them revealed REM abnormalities, including increase in REM phasic and tonic muscle activities, which were associated with brief body movement during REM sleep. Four of the 11 subjects had comorbid OSAS. The REM abnormalities persisted with the use of continuous positive airway pressure. The remaining 2 subjects did not have any REM abnormalities in PSG assessments.

DISCUSSION

Parasomnia in Psychiatric Outpatients: An Overlooked Condition

Epidemiologic surveys investigating parasomnia among the psychiatric population are very limited. There were only small-scale surveys, which employed self-reported questionnaires, suggesting an increase in prevalence of parasomnias among specific clinical groups.[5,26] To our knowledge, this is the first cross-sectional study of parasomnia including sleepwalking, SRED, and SRI in general psychiatric outpatient populations by self-reported questionnaire and confirmation by clinical interview.

In our study, we found that these conditions were not uncommon. For sleepwalking, our lifetime prevalence of 8.5% was higher than the general population of 2% to 3.9%.[2,27] SRI and sleep violence were much more common than expected, with an estimated lifetime prevalence of 21.0% and 3.6%, respectively, and a 1-year prevalence of 8.8% and 2.5%, respectively, compared with a lifetime prevalence rate of 2.1% for SRI in the general population.[28] Regarding SRED, our finding of lifetime prevalence of 4.0% is comparable to the literature finding of 3.4% in depressive disorder,[5] but it is lower than that found in subjects with eating disorders, who had prevalence rates from 8.7% to 16.7% in outpatient and inpatient settings, respectively.[5]

The lifetime and 1-year prevalence rates of RSBD-like disorder were much higher than that of typical RSBD in local population (0.38%).[29] Compared to subjects with typical RSBD, our subjects constituted a younger population with slightly female predominance and were not associated with any neurodegenerative disease. Case reports of SSRI-related RSBD also showed similar clinical demographic features to those found in our subjects.[17,18] The exact relationship between the drug-related RSBD-like disorder and typical RSBD (old age, male predominance, association with neurodegenerative disease) was not certain. It remained to be determined whether RSBD-like disorder represented a variant or subgroup of typical RSBD or an independent disorder related to a unique mechanism of some psychotropics (see below).

The consequences of these conditions could be serious. Our subjects sustained injuries of different degrees during parasomniac episodes, including bruises, laceration, sprain, and fractures. They also inflicted injuries on others with serious acts, such as kicking, hitting, and strangling bed partners. Dangerous acts, including cooking, burning pot on stove, and consuming frozen food under impaired consciousness level, had been reported. Despite the high prevalence and potential serious consequences, these conditions remained hidden and unattended. We observed that the majority of patients did not report their sleep problems to their doctors. The underreporting could be related to the episodic nature of the conditions and unawareness of its potential serious consequences by both patients and doctors.

Parasomnia and Mental Illness

In our study, subjects having depressive spectrum disorder had higher risk of having sleepwalking, SRED, SRI, and RSBD-like disorder. Sleepwalking was reported to be associated with affective disorder,[3] and adult-onset sleepwalking was associated with increased life events and mental stress.[4] In addition, case reports on depression comorbid with RSBD reports have been reported.[19] The apparent association of depression with these parasomnias could be related to mental stress, which serves as a common precipitating factor for both illnesses. Alternatively, the association of depression and parasomnia could be mediated through the effect of sleep disturbances and psychotropic medications, as reflected in our multivariate analysis.

Subjects with psychotic spectrum disorder were less likely than those with depressive spectrum disorder to have the parasomnias. One possible reason is that they might underreport their sleep problems as reflected by their higher refusal rate. Alternatively, the better-refined definitions of psychiatric and sleep disorders, detailed recording of sleep psychopathology, and use of psychotropics in our study may suggest that these parasomnias would indeed be less common in people with psychotic spectrum disorder.

Parasomnia and Sleep Disturbance

Various sleep disturbances were previously reported in the literature to be associated with parasomnias. Sleep-talking and bruxism were more prevalent in sleepwalking,[3] while SRED was associated with insomnia and sleep apnea.[14,30–32] In subjects with RSBD, nightmares with content of aggression were frequently reported.[33] Our study highlighted the findings that these parasomnias were highly comorbid with other sleep disturbances. These disturbances could contribute to the parasomnias via sleep disruptions and fragmentations. Thus, systematic inquiry and appropriate management of concurrent sleep disturbances are equally important when dealing with these parasomnias.

Parasomnia and Psychotropic Medication

Our study suggested that psychotropics were strongly associated with sleepwalking, SRED, and RSBD-like disorder. The results provided further evidence and clues about drug-associated parasomnia. Among all types of medications, sedative antidepressants such as tricyclics and nonbenzodiazepine hypnotics were associated with higher risk of sleepwalking. The association could signify underlying sleep disturbances, such as insomnia and nightmares, and hence subjects were more likely to be prescribed these sedative medications. Alternatively, the association could be accounted for by their specific pharmacologic effect. Tricyclic antidepressants have limited effect on NREM sleep, but their anticholinergic and antihistamine effect may impair arousal. Nonbenzodiazepine hypnotics, including both zolpidem and zopiclone, are short-acting hypnotics that act through γ-aminobutyric $acid_A$ ($GABA_A$) receptors. They are associated with amnesic effect and possible modulation of slow wave sleep at therapeutic doses,[34] with a consequent increase in propensity for triggering sleepwalking.

Psychotropic medications, particularly SSRIs, sedative antidepressants, and zolpidem, were strongly associated with SRED. Among all the psychotropics, zolpidem had the highest OR and strongest association with SRED. One of 7 subjects taking zolpidem developed SRED. Those at risk were more likely taking zolpidem regularly rather than on an as-necessary basis. As mentioned above, nonbenzodiazepine hypnotics have increased propensity for sleepwalking. However, zopiclone, which lacks selectivity over α_1 subunit of $GABA_A$ receptors as in zolpidem, was apparently not associated with SRED. This suggested that zolpidem triggered SRED, not only by increasing the susceptibility of sleepwalking, but also via other mechanisms, most likely hyperphagia. In this regard, zolpidem was reported to induce hyperphagic response in animals.[35] The neuropharmacologic effect of zolpidem on appetite and SRED certainly warrants further research. Antidepressants might also contribute to SRED by sleep disruption and hyperphagia.[36–38] Thus, the multifactorial

etiology of drug-related SRED might probably act through different and/or synergistic mechanisms: sleep disruption by SSRIs,[39] impaired arousal by tricyclics, amnesia and a possible modulation of slow wave sleep by zolpidem, and hyperphagic response by both antidepressants and zolpidem.

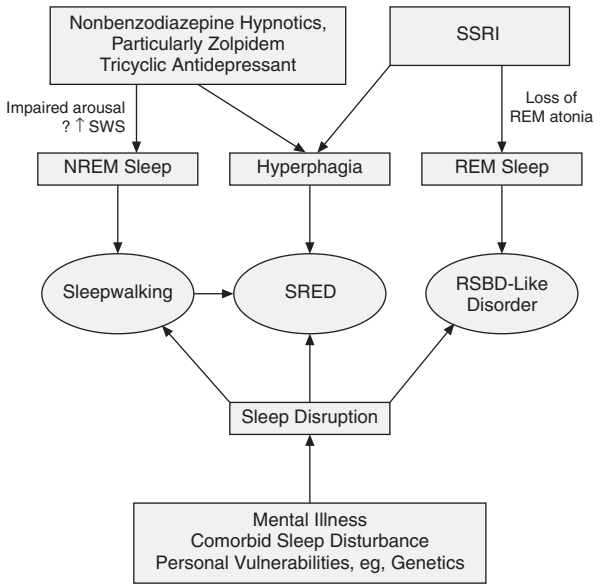
Our results suggested that RSBD-like disorder was predominantly associated with SSRIs, currently one of the commonly prescribed antidepressants. SSRIs have REM suppressant effect, and they are used for treatment of REM sleep-related disorders, such as sleep paralysis and cataplexy.[40,41] However, in concordance with the increasing reports of SSRI-related RSBD-like disorder,[17] our data gave further evidence that SSRIs could enhance the risk of RSBD-like symptoms.[18] The exact mechanism was uncertain, but SSRIs were reported to be associated with lesser but more vivid and intense dream recalls[42] and loss of REM sleep atonia in polysomnography,[18] a hallmark feature of RSBD. The disinhibition of REM sleep atonia allows dream enactment in vulnerable subjects, particularly in those having recurrent emotionally charged and aggressive dreams. However, we observed that only a proportion of those taking SSRIs developed RSBD-like disorders. Further studies looking into dosage effect, subtypes of SSRIs, and individual vulnerabilities may help in clarifying the association, as well as delineating the relationship between these drug-related RSBD-like disorders and typical RSBD.

LIMITATION

Our study had some shortcomings. As in other parasomnia studies, the limited awareness of parasomnia by ones with parasomnia might predispose them to some recall biases, albeit we attempted to get collateral information from their family or cohabitants. The overall response rate for phases 1 and 2 studies was modest and that of phase 3 was rather low. However, PSG evidence is not essential for the diagnosis of most NREM-related parasomnias as it is episodic, with marked night-to-night variation. On the contrary, definitive diagnosis of RSBD required PSG evidence. Nearly half of the RSBD-like–disordered subjects completed the phase 3 studies, and those who completed showed high percentage of REM abnormality, which further supported and confirmed the clinical diagnoses. However, the PSG was not blindly scored and we did not quantify the REM phasic and tonic activities. This could potentially lead to diagnostic bias of the PSG findings. Further comparative quantifying electromyogram study of the PSG features for both drug-related and typical RSBD would be needed.

Regarding the prescription pattern, the percentage of psychotropic usage in our study was comparable to other Asian countries.[43,44] Nonetheless, the analysis of psychotropic usage and parasomnias was not a real-time association, and it was difficult to ascertain the cause-consequence effect. Nevertheless, we attempted to evaluate the impact of psychotropics only in those having active parasomnia in recent 1 year, and the psychotropics used in the same period were recorded in detail. As limited by this study's cross-sectional design, further prospective and intervention studies are required for better establishment of causation and delineation of the etiological factors.

Figure 2. Proposed Mechanisms of Interacting Effects of Mental Illness, Sleep Disturbance, and Psychotropic Medication in Parasomnias



Abbreviations: NREM = nonrapid eye movement, REM = rapid eye movement, RSBD-like disorder = rapid eye movement sleep behavior–like disorder, SRED = sleep-related eating disorder, SSRI = selective serotonin reuptake inhibitor, SWS = slow wave sleep.

In summary, parasomnias, as characterized by dramatic movement, including sleepwalking, SRED, RSBD-like disorder, and SRI, were prevalent in a psychiatric population. The etiology of parasomnia in psychiatric populations is complex. Mental illness, sleep disturbances, and psychotropics played interacting roles in precipitating the conditions (Figure 2). Clinicians should be aware of these hidden, common, and potentially dangerous parasomnias with appropriate management and warning to patients.

Drug name: zolpidem (Ambien and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, trazodone is not approved by the U.S. Food and Drug Administration for the treatment of insomnia, and mianserin and zopiclone are not approved for use in the United States.

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