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Association Between Specific Insomnia Symptoms and Aggression in Chinese Patients with Chronic Schizophrenia: A Large-Scale Cross-Sectional Study

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Purpose: Aggression is a significant issue in schizophrenia, with insomnia identified as a modifiable risk factor. However, research often treats insomnia as a single construct, neglecting potential differences among its symptoms: difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), and early morning awakening (EMA). This study examined these distinct associations in a large sample of Chinese patients with chronic schizophrenia.

Patients and methods: A total of 702 inpatients with chronic schizophrenia was approached and screened. Among them, 31 were excluded due to missing data, resulting in a final sample size of 671. Aggression was assessed with the Modified Overt Aggression Scale, insomnia symptoms with the Insomnia Severity Index, and psychopathology with the Positive and Negative Syndrome Scale (PANSS). Logistic regression models examined associations between insomnia symptoms and aggression, controlling for theory-driven set of demographic and clinical variables identified from the literature as potential confounders (age, gender, illness duration, PANSS factor scores, antipsychotic dosage, clozapine use, polypharmacy, and sleep medication usage).

Results: The prevalence of aggression, DIS, DMS, and EMA were as follows: 14.6% (n=98), 14.2% (n=95), 11.3% (n=76), and 9.6% (n=64). One-fifth of the patients used sleep medication. Unadjusted analyses linked all three insomnia symptoms to increased aggression risk, with DIS showing the strongest association (Crude odds ratio =4.18, 95% CI=2.55–6.86, p<0.001). After full adjustment, only DIS remained independently associated (Adjusted odds ratio=3.81, 95% CI=1.77–8.21, p<0.001). Further analysis revealed DIS rather than DMS or EMA was uniquely linked to all aggression domains: verbal, property, auto-, and physical aggression.

Conclusion: DIS, rather than other insomnia symptoms, shows a consistent and independent association with multiple forms of aggression, highlighting its clinical significance in managing chronic schizophrenia. Clinical assessment should therefore differentiate between insomnia symptoms, and longitudinal and interventional studies are needed to confirm this association and explore its therapeutic implications.

Keywords: insomnia, aggressive behavior, schizophrenia, difficulty initiating sleep

Introduction

Aggression in individuals with schizophrenia is a major clinical and public health concern, contributing to adverse patient outcomes, caregiver burden, and significant social stigma.[1,2] While prevalence rates vary widely, meta-analysis indicates a substantially elevated prevalence, suggesting that up to one-third of patients may exhibit aggressive behaviors.[2] This problem is even more severe in China. Recent global estimates suggest that China bears one of the largest national burdens of schizophrenia, with over 5.3 million affected individuals and age-standardized prevalence and disability-adjusted life-year rates exceeding global averages, both of which continue to rise.[3] In parallel, epidemiological meta-

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analysis has shown that Chinese patients exhibit a particularly high prevalence of aggression, with meta-analytic data indicating rates around 35–50% among inpatients, much higher than those reported in many other countries.[2] Even among Chinese patients with chronic or stable illness, the prevalence remains a clinical concern, affecting approximately 16% of this population.[4–6] Identifying modifiable risk factors is therefore a clinical priority to inform targeted preventive strategies and improve patient management.

In recent years, there has been an increasing awareness of the significant connection between insomnia and a variety of negative clinical outcomes in schizophrenia.[7–13] Our prior findings indicated that insomnia was tightly associated with more serious symptoms, suicidality, and weakened neurocognition.[7,10,11,13–15] Furthermore, emerging studies have consistently demonstrated insomnia as a significant contributor to aggression in schizophrenia.[4,6,16] A longitudinal evidence suggests that insomnia prospectively increases the likelihood of violent behavior by 38%.[17] The neurobiological underpinnings of this relationship are thought to involve multiple pathways, including heightened emotional dysregulation, impaired impulse control,[18,19] increased negative affect, and dysregulation of neurobiological systems (eg, serotonin, cortisol),[20,21] which are integral to modulating both sleep and aggression.

Despite the established link between global insomnia and aggression, a critical gap remains in understanding how specific insomnia symptoms relate to this outcome. Most research has treated insomnia as a monolithic construct, overlooking the potential differential impacts of its core symptoms: difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), and early morning awakening (EMA). Emerging research suggests these symptoms have distinct clinical correlates in schizophrenia. For instance, data from the Clinical Antipsychotic Trials of Intervention Effectiveness showed that initial (DIS) and terminal (EMA) insomnia were differentially associated with psychopathology and suicidal behaviors.[22] In another cohort of individuals of clinical high risk for psychosis, only terminal insomnia was linked to suicide attempts.[23] In contrast, a network analysis of Chinese patients with schizophrenia identified DIS as a key "bridge symptom" connecting insomnia to broader psychiatric symptoms.[11] These nuanced evidence underscores the necessity of moving beyond a unitary view of insomnia to investigate symptom-specific relationships with critical outcomes like aggression.

From a biological perspective, the three types of insomnia exhibit different neurobiological correlates.[24–27] DIS is primarily characterized by a state of pre-sleep hyperarousal, involving increased activation of limbic structures such as the amygdala and anterior cingulate cortex, together with impaired top-down inhibitory control from the prefrontal cortex. This pattern contributes to emotional instability, impulsivity, and exaggerated threat perception. In contrast, DMS is associated with fragmentation of sleep architecture and dysregulation of the hypothalamic–pituitary–adrenal axis, marked by elevated nocturnal cortisol and autonomic imbalance. Early morning awakening is fundamentally a disorder of circadian misalignment, where a phase-advanced internal clock prematurely initiates the hormonal cascade for wakefulness, terminating sleep hours before desired. These distinct pathophysiological profiles suggest that specific insomnia symptoms may differentially influence emotional regulation and behavioral control. Therefore, it is plausible that difficulty initiating sleep—characterized by hyperarousal and prefrontal-limbic dysregulation—exerts a stronger association with aggression in patients with schizophrenia.

Previous studies have shown that both insomnia and aggression in schizophrenia are influenced by multiple demographic and clinical factors. Insomnia tends to be more prevalent among younger individuals and those with shorter illness duration, higher positive symptom burden, or depressive features.[10–12] Similarly, aggression has been associated with younger age, male sex, shorter illness duration, and elevated levels of positive and agitation symptoms.[16,28] Medication-related factors, such as clozapine treatment or sleep medication, have also been linked to aggression and insomnia modulation.[1,29] Incorporating these factors as covariates is therefore essential to clarify whether specific insomnia symptoms are independently associated with aggression beyond the effects of psychopathology or treatment characteristics.

Therefore, we conducted this explanatory analysis in a large, well-characterized sample of Chinese patients with chronic schizophrenia. Our primary aims were to: (1) assess the prevalence of aggression and specific insomnia symptoms (DIS, DMS, and EMA); (2) investigate and compare the associations between each insomnia symptom and aggression; and (3) identify which symptom, if any, remained independently associated with aggression after accounting

for key demographic and clinical variables. We hypnotized that: (1) Patients with aggression would show higher levels of insomnia; (2) DIS would exhibit a stronger association with aggression compared to DMS and EMA.

Methods

Study Procedure and Participants

The study procedure was shown in Figure 1. This study is a secondary analysis of data originally collected for a large-scale, cross-sectional investigation into the association between insomnia and suicidal ideation in schizophrenia.[7] Although drawn from the same comprehensive database, the current study was specifically designed to provide novel insights into a distinct scientific question: the relationship between individual insomnia symptom profiles and aggression. It enrolled inpatients with chronic schizophrenia from the psychiatry departments of the following hospitals across China during 2019: Chaohu Hospital of Anhui Medical University, The Third People's Hospital of Changshu, The Third People's Hospital of Ganzhou, The Affiliated Brain Hospital of Guangzhou Medical University, Hebei Province Veterans

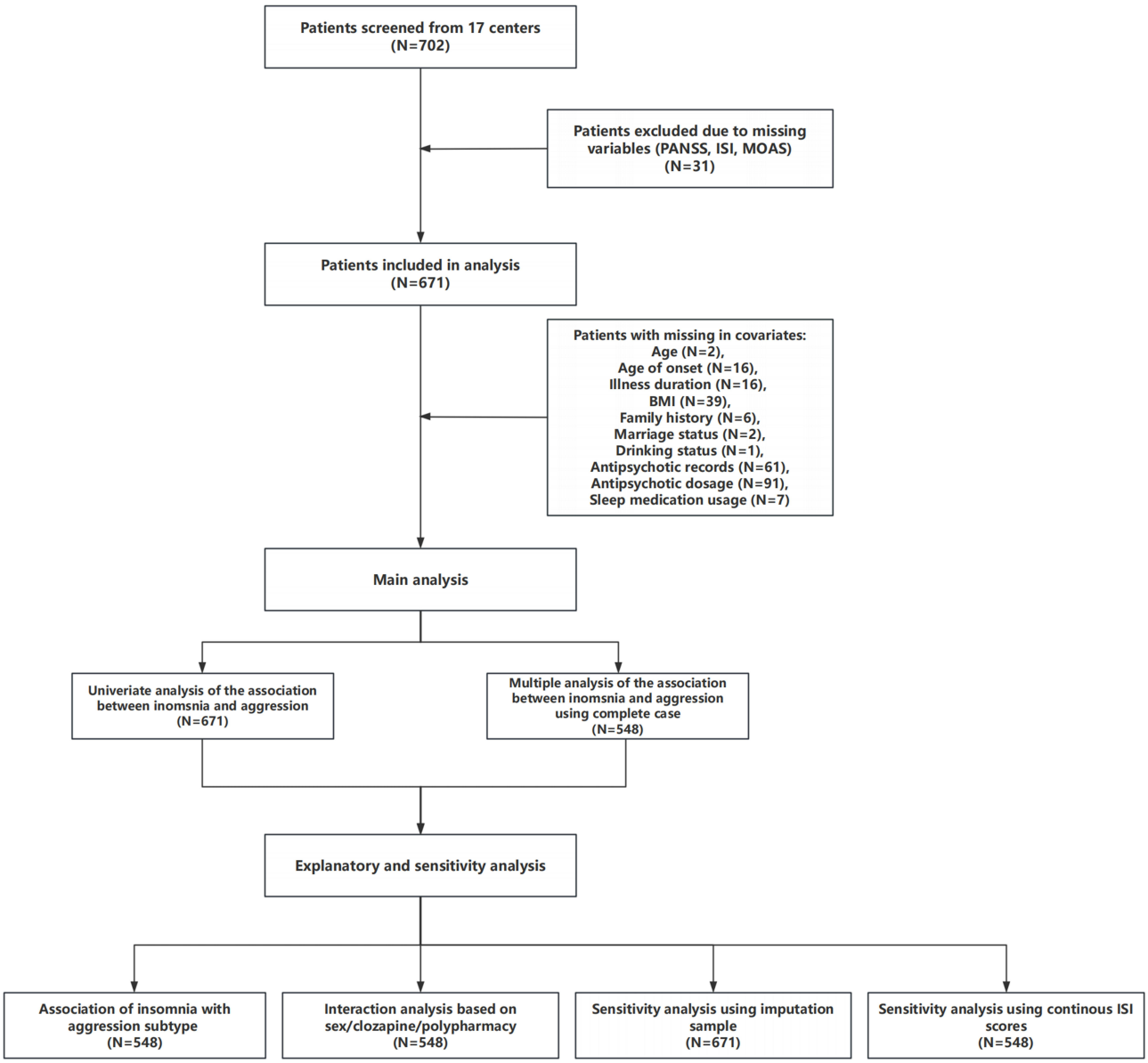

Figure 1 Study flowchart.

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Hospital, Mental Health Centre of Jingzhou, Nanning Fifth People's Hospital, Ning An Hospital of Ningxia, Shanghai Pudong New Area Mental Health Centre, Shanghai Putuo District Mental Health Centre, Shandong Mental Health Centre, Shanxi Province Veterans Hospital, Shenyang Anning Hospital, Suzhou Guangji Hospital, Wenzhou Kangning Hospital, Wuhan Mental Health Centre and The Third Affiliated Hospital of Sun Yat-sen University. All hospitals were academic hospitals.

Eligibility was determined through face-to-face interviews conducted by two independent, trained psychiatrists using the Structured Clinical Interview for DSM-IV (SCID). The inclusion criteria were: (1) a DSM-IV diagnosis of schizophrenia verified by the SCID; (2) a disease duration exceeding one year; (3) clinical stability and being competent to make a decision to participate in the study., indicated by a fixed antipsychotic treatment plan for at least six months before the study and no major fluctuations in psychiatric symptoms in the two weeks leading up to participation; and (4) Han nationality, aged 18 to 70 years. The SCID was additionally employed to screen out participants with other primary Axis I mental health conditions, including bipolar disorder, depressive psychosis, or schizoaffective disorder. Further exclusion factors comprised active substance abuse (though tobacco use was allowed), current pregnancy or lactation, and any serious or uncontrolled medical illnesses (eg, malignancies, traumatic brain injury, or active infections).

All participants were fully informed of the study objective. The participation was voluntary, and they could withdraw at any time. Written informed consent was obtained from all participants prior to enrollment. This study complied with the Declaration of Helsinki and was reviewed by the Institutional Review Board of the Institute of Psychology, Chinese Academy of Sciences (H18031); this approval was granted while the corresponding author (Xiangyang Zhang) was employed at this institution.

Measurements

Demographic and Clinical Information

Demographic and clinical information was obtained through a custom-designed questionnaire and medical record review. The collected data encompassed age, gender, educational attainment, marital status, body mass index (BMI), age at symptom onset, duration of illness, and smoking and alcohol consumption habits. Smoking status was classified into non-smoker, former smoker, or current smoker in accordance with World Health Organization guidelines. Antipsychotic medication dosages were converted to chlorpromazine equivalents to standardize comparisons.[30] The use of sleep medication (a binary variable encompassing Z-drugs, benzodiazepines and other adjunctive sedatives), current clozapine use (yes/no), and antipsychotic polypharmacy (yes/no) was recorded.

Psychiatric Symptoms

Psychiatric symptom severity was evaluated by two trained clinicians using the Positive and Negative Syndrome Scale (PANSS), a 30-item instrument comprising three subscales: positive (7 items), negative (7 items), and general psychopathology (16 items).[31] The assessment demonstrated strong inter-rater reliability (correlation coefficient > 0.8). For this analysis, PANSS items were structured according to a validated 5-factor model:[10] positive (P1, P3, P5, P6, G9), negative (N1, N2, N3, N4, N6, N7, G7, G16), mood (G1, G2, G3, G4, G6), hostility/excitement (P4, P7, G8, G14), and cognition (P2, N5, G5, G10, G11, G12, G13, G15).

Insomnia

Specific symptoms of nocturnal insomnia were evaluated using the first three items of the Insomnia Severity Index (ISI).[32] These items assessed the severity of difficulty initiating sleep, difficulty maintaining sleep, and early morning awakening. The severity of each symptom over the last two weeks was rated on a 5-point scale from 0 ("no") to 4 ("extremely severe"). For analytical purposes, the presence of a specific insomnia symptom was defined by a score of ≥2 ("Moderate") on the corresponding item, a method utilized in previous studies of this population.[12,13]

Aggression

Aggression was assessed using the Modified Overt Aggression Scale (MOAS), a clinician-rated instrument that measures the severity of a patient's aggressive behavior over the preceding week.[33,34] The scale evaluates four domains: verbal aggression, aggression against property, auto-aggression, and physical aggression. Each domain is scored from 0 to 4

based on the severity of the behavior. A total score is calculated by applying a weighted system: (Verbal Aggression Score × 1) + (Aggression Against Property Score × 2) + (Auto-aggression Score × 3) + (Physical Aggression Score × 4). Ratings were completed by trained clinical staff based on direct observation and a review of patient records. A total MOAS score of ≥3 was used as the cutoff to define the presence of clinically significant aggressive behavior.[35] For our exploratory analysis of individual aggression domains, the presence of a specific domain was defined by a score of ≥1 on the corresponding subscale. All clinical raters underwent a standardized training program on the administration of the SCID, PANSS and MOAS, which included reviewing instructional videos, scoring practice cases, and achieving an inter-rater reliability of ICC > 0.80 against a gold-standard rater before the commencement of the study. In our study, the inter-rater correlation coefficient for the PANSS and MOAS exceeded 0.80.

Statistical Analysis

Descriptive statistics are presented as means ± standard deviations for continuous variables and counts (percentages) for categorical variables. Group differences between patients with and without aggression were assessed using Student's t-tests for continuous variables and Chi-square tests for categorical variables. To account for multiple comparisons in these initial analyses, a Bonferroni correction was applied, setting the significance threshold at $p < 0.0024$ (0.05/21 tests).

The primary analysis employed hierarchical logistic regression to examine the association between insomnia symptoms (DIS, DMS, EMA) and aggression (MOAS ≥3). Three models were constructed: Model 1 (unadjusted); Model 2 (mutually adjusted for all three insomnia symptoms); and Model 3 (fully adjusted for a theory-driven set of demographic and clinical covariates, including age, gender, illness duration, PANSS factor scores, antipsychotic dosage, clozapine use, polypharmacy, and sleep medication). Collinearity was assessed in Model 3 using Variance Inflation Factors (VIFs), all of which were below 5, indicating no significant multicollinearity. Model diagnostics, including the Hosmer-Lemeshow test and Area Under the Curve (AUC), were calculated for the final model.

To test the robustness of our findings, we conducted several sensitivity analyses: (1) re-running the primary models on a dataset with missing medication variables imputed via the missRanger package (using a random forest algorithm, seed=123); (2) testing for effect modification by including interaction terms between DIS and key clinical variables (gender, clozapine use, polypharmacy); and (3) analyzing insomnia symptoms (ISI scores) as continuous variables.

An exploratory analysis investigated the associations between specific insomnia symptoms and the four individual aggression domains (verbal, property, auto-aggression, physical), with each domain coded as present if its score was ≥1. These models were adjusted for the same covariates as Model 3.

The primary analyses were conducted using a complete-case approach, excluding cases with missing data. To assess the potential impact of missing data, we performed a sensitivity analysis. Missing data were imputed using the missRanger package in R (seed=123), which employs a random forest algorithm. The primary regression models were then re-run on the fully imputed dataset.

All analyses were performed using a complete-case approach for the primary models, with a two-tailed significance level of $p < 0.05$. Statistical computations were conducted in R (version 4.2.0) utilizing the stats, gtsummary and missRanger packages.[36,37] The R code could be found in the supplementary materials.

Results

Sample Characteristics

Of the 702 eligible patients initially approached, 31 were excluded due to missing data on the PANSS, MOAS, or insomnia measures, resulting in a final sample of 671 participants for analysis (Table 1). The mean age of the sample was 42.76 ± 13.26 years, and the cohort was predominantly male (68.5%). Participants had an average of 9.30 ± 2.97 years of formal education. The mean age of illness onset was 24.68 ± 8.00 years, with a mean illness duration of 18.03 ± 12.35 years.

Medication data were available for 610 participants. The distribution of antipsychotic medications was as follows: 217 with clozapine, 210 with risperidone, 149 with olanzapine, 135 with aripiprazole, 78 with quetiapine, 42 with amisulpride, 36 with chlorpromazine, 19 with ziprasidone, 16 with sulpiride, 14 with perphenazine, 9 with haloperidol, 4

Table 1 Demographic and Clinical Characteristics Between Patients with and Without Aggression

Variables	Total (n = 671)	Without Aggression (n = 573)	With Aggression (n = 98)	*P*
Gender, n(%)				0.252
Male	459 (68.51)	387 (67.66)	72 (73.47)	
Female	211 (31.49)	185 (32.34)	26 (26.53)	
Age, Mean ± SD	42.76 ± 13.26	43.56 ± 13.31	38.08 ± 11.98	**<0.001**
Education year, Mean ± SD	9.30 ± 2.97	9.25 ± 2.86	9.59 ± 3.56	0.374
Age of onset, Mean ± SD	24.68 ± 8.00	24.81 ± 7.84	23.89 ± 8.90	0.303
Duration, Mean ± SD	18.03 ± 12.35	18.68 ± 12.52	14.16 ± 10.57	**<0.001**
Daily antipsychotic dosage, Mean ± SD	429.34 ± 265.03	424.20 ± 253.99	461.50 ± 325.76	0.243
Polypharmacy, n(%)				0.203
Without	311 (50.98)	259 (49.90)	52 (57.14)	
With	299 (49.02)	260 (50.10)	39 (42.86)	
Clozapine use, n(%)				0.423
Without	393 (64.43)	331 (63.78)	62 (68.13)	
With	217 (35.57)	188 (36.22)	29 (31.87)	
Sleep Medicine, n(%)				0.27
Without	541 (80.63)	458 (79.93)	83 (84.69)	
With	130 (19.37)	115 (20.07)	15 (15.31)	
Married Status, n(%)				0.544
Unmarried	526 (78.62)	452 (79.02)	74 (76.29)	
Married	143 (21.38)	120 (20.98)	23 (23.71)	
Family history, n(%)				0.902
Without	539 (81.05)	464 (80.98)	75 (81.52)	
With	126 (18.95)	109 (19.02)	17 (18.48)	
Drink, n(%)				0.129
Without	597 (89.10)	514 (89.86)	83 (84.69)	
With	73 (10.90)	58 (10.14)	15 (15.31)	
Smoking, n(%)				0.484
Non-smoker	388 (57.82)	328 (57.24)	60 (61.22)	
Ex-smoker	78 (11.62)	65 (11.34)	13 (13.27)	
Current smoker	205 (30.55)	180 (31.41)	25 (25.51)	
Body mass index, Mean ± SD	24.18 ± 4.86	24.32 ± 4.90	23.29 ± 4.53	0.062
PANSS factor				
Positive, Mean ± SD	13.46 ± 6.16	12.84 ± 6.05	17.06 ± 5.56	**<0.001**
Depres, Mean ± SD	10.01 ± 4.44	9.64 ± 4.25	12.20 ± 4.89	**<0.001**
Negative, Mean ± SD	22.70 ± 7.58	22.57 ± 7.65	23.45 ± 7.18	0.29
Excited, Mean ± SD	8.02 ± 3.81	7.55 ± 3.58	10.77 ± 3.97	**<0.001**
Cognitive, Mean ± SD	25.15 ± 8.03	24.74 ± 8.10	27.52 ± 7.19	**0.002**

Note: Some data contain missing values. Bold suggests the statistical significance that passed the multiple correction.
Abbreviations: PANSS, Positive and Negative Syndrome Scale; SD, standard deviation.

with paliperidone, and 3 with perospirone. A notable portion of participants (49.0%; n=299) were receiving polypharmacy with multiple antipsychotic medications. The mean daily antipsychotic dosage, calculated in chlorpromazine equivalents, was available for 596 participants. The "sleep medication" variable was coded as a binary indicator (yes/no). Data on sleep medication were available for 664 participants; approximately one-fifth were prescribed such medication.

Comparison of Patients with and without Aggression

The prevalence of any clinically significant aggression (MOAS score at 3 or above) was 14.6% (n=98). The most common form of aggression was verbal (22.9%; n=153), followed by aggression against property (7.7%; n=52), physical aggression (7.5%; n=50), and auto-aggression (4.9%; n=33). When considering the number of co-occurring aggression

domains, the distribution was as follows: 72.7% (n=488) exhibited no aggression, 16.4% (n=110) exhibited one domain, 6.9% (n=46) exhibited two domains, 3.3% (n=22) exhibited three domains, and 0.7% (n=5) exhibited all four domains.

A comparison of demographic and clinical characteristics between patients with and without aggression is detailed in Table 1. The aggressive group was significantly younger (38.08 ± 11.98 vs 43.56 ± 13.31 years) and had a shorter duration of illness (14.16 ± 10.57 vs 18.68 ± 12.52 years) than the non-aggressive group. Significant differences in psychopathology were also observed; the aggressive group had higher mean scores on the PANSS positive (17.06 ± 5.56 vs 12.84 ± 6.05), depression (12.20 ± 4.89 vs 9.64 ± 4.25), excitement (10.77 ± 3.97 vs 7.55 ± 3.58), and cognitive subscales (27.52 ± 7.19 vs 24.74 ± 8.10). All these differences remained significant after multiple correction. No significant differences were identified between the two groups regarding gender, education level, age of onset, antipsychotic dosage, BMI, PANSS negative scores, or marital, smoking, and drinking status.

Association of Insomnia Symptoms with Aggression

The prevalence of specific insomnia symptoms was 14.2% for DIS, 11.3% for DMS, and 9.6% for EMA. One-fifth of the patients suffered from at least one type of insomnia. As shown in Figure 2, the prevalence of both DIS (33.7% vs 10.8%) and DMS (22.5% vs 9.4%) was significantly higher in the aggressive group. A similar trend was observed for EMA (16.3% vs 8.4%), though this association did not survive Bonferroni correction. Overall, patients with aggression were more than twice as likely to suffer from any insomnia symptom (42.9% vs 17.5%, p′<0.05). A detailed distribution of ISI item score and aggression could be found at Supplementary Tables S1–S3.

Hierarchical logistic regression analysis was conducted to determine the association between insomnia symptoms and aggression (Figure 3). In the unadjusted analysis (Model 1), all three symptoms were significantly associated with aggression, with DIS showing the strongest link (Crude Odds Ratio [COR] = 4.18, 95% CI = 2.55–6.86, p < 0.001). When all three symptoms were included simultaneously (Model 2), only DIS remained a significant predictor (Adjusted Odds Ratio [AOR] = 3.78, 95% CI = 2.07–6.88, p < 0.001). In the fully adjusted model (Model 3), DIS persisted as an independent predictor of aggression (AOR = 3.81, 95% CI = 1.77–8.21, p <0.001). In the final model, age (AOR = 0.96, 95% CI = 0.91–0.99, p = 0.042), higher scores on the PANSS positive symptom (AOR = 1.06, 95% CI = 1.01–1.13, p =

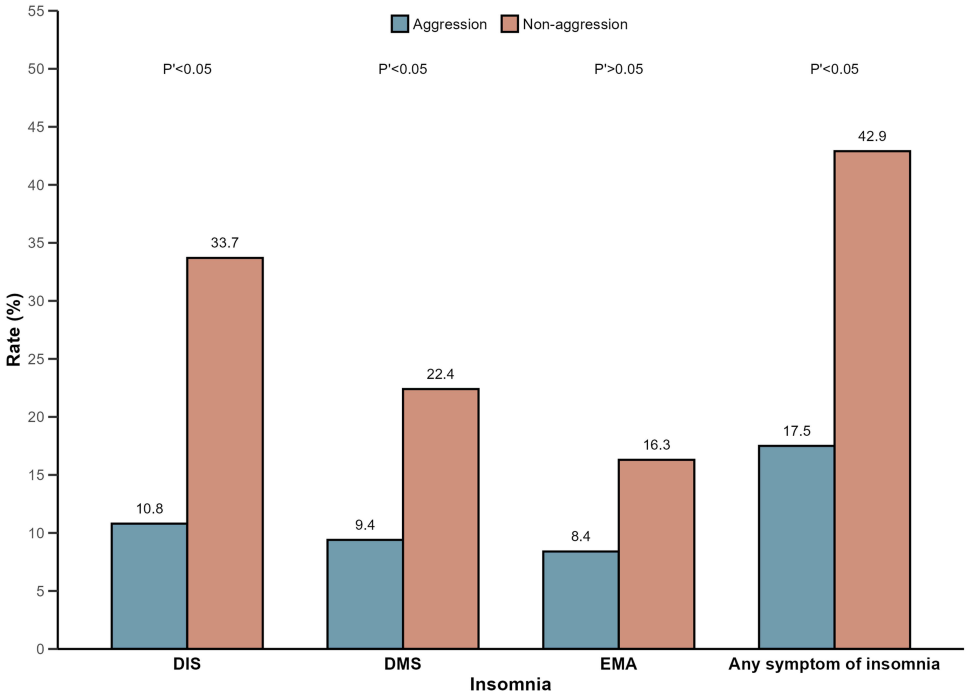

Figure 2 Association of insomnia with aggression.
Abbreviations: DIS, difficult initialing sleep; DMS, difficult maintaining sleep; EMA, early morning awakening.

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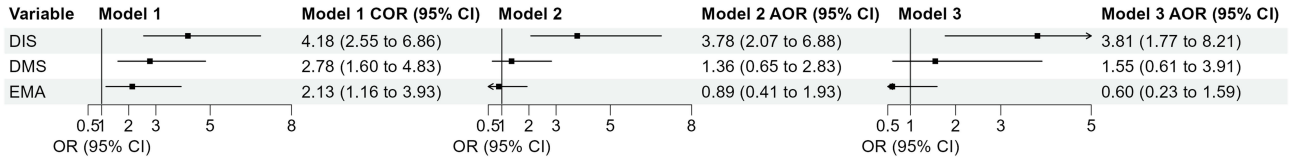

Figure 3 Univariate and multiple analysis of the association between insomnia and aggression.
Note: Model 1 is unadjusted; Model 2 adjusted for the presence of all three insomnia subtypes simultaneously to assess their independent effects Model 3 additionally adjusted for age, gender, illness duration, PANSS factor scores, antipsychotic dosage, clozapine use, polypharmacy, and sleep medication usage on the basis of Model 2.
Abbreviations: DIS, difficult initialing sleep; DMS, difficult maintaining sleep; EMA, early morning awakening; COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval.

0.027) and excitement symptoms (AOR = 1.18, 95% CI = 1.08–1.29, p < 0.001) were also independently associated with aggression (Table 2). Holding all other covariates at their mean values, the probability of aggression was 9.6% for patients without DIS and 37.5% for patients with DIS, yielding an absolute risk difference of 27.9%. All VIF values were below 5, indicating no multicollinearity (detailed results shown in Supplementary Table S4). The Hosmer-Lemeshow test was non-significant (p=0.82), indicating good model fit. The Akaike Information Criterion was 374.68, and the Area Under the ROC Curve was 0.82 (95% CI: 0.78–0.87), demonstrating excellent discrimination.

Sensitivity and Explanatory Analysis

The association between DIS and aggression demonstrated robustness across multiple sensitivity analyses. When missing medication data were handled using imputation (Table S5), DIS remained significantly associated with aggression (AOR = 2.82, 95% CI: 1.41–5.62, p =0.003). Formal tests for effect modification revealed no significant interactions between DIS and gender, clozapine use, or polypharmacy (shown in Table S6, all p for interaction > 0.05), indicating the consistency of this association across these clinical subgroups. Furthermore, when analyzed as a continuous variable (Table S7), each one-point increase in DIS severity was associated with a 46% increase in the odds of aggression (AOR = 1.46, 95% CI: 1.01–2.12, p = 0.045).

An exploratory analysis examined the association between insomnia symptoms and the four dimensions of aggression (Table 3). After full adjustment, DIS was significantly associated with an increased likelihood of all four domains: verbal aggression (AOR = 2.58, 95% CI = 1.43–4.64, p =0.002), aggression against property (AOR = 2.47, 95% CI = 1.08–5.67, p =0.033), auto-aggression (AOR = 2.73, 95% CI = 1.07–6.96, p =0.035), and physical aggression (AOR = 4.41, 95% CI = 1.96–9.93, p <0.001). In contrast, neither DMS nor EMA showed a significant association with any individual aggression dimension.

Discussion

To our knowledge, this is the first study to systematically examine the differential associations between specific insomnia symptoms and aggression in a large sample of patients with chronic schizophrenia. The principal finding is that difficulty initiating sleep was uniquely and independently associated with an increased risk of aggression. This relationship remained robust after controlling for a comprehensive range of demographic and clinical covariates and extended across

Table 2 Multivariable Logistic Regression Analysis of Factors Associated with Aggression (Model 3, Fully Adjusted, N=548)

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Difficulty Initiating Sleep	3.81	1.77–8.21	< 0.001
Age	0.96	0.91–0.99	0.042
PANSS Positive Symptoms	1.06	1.01–1.13	0.027
PANSS Excitement Symptoms	1.18	1.08–1.29	< 0.001

Note: The model was adjusted for all three insomnia symptoms, demographic variables (age, gender), and clinical covariates (illness duration, PANSS factor scores, antipsychotic dosage, clozapine use, polypharmacy, and sleep medication usage). Only statistically significant predictors (p < 0.05) from the full model are displayed here for clarity.
Abbreviations: AOR, Adjusted Odds Ratio; PANSS, Positive and Negative Syndrome Scale.

Table 3 Exploratory Analysis of the Association Between Insomnia Symptoms and Specific Domains of Aggression

	Verbal (AOR,95% CI)	Property (AOR,95% CI)	Auto (AOR,95% CI)	Physical (AOR,95% CI)
DIS	2.58 (1.43 ~ 4.64) **	2.47 (1.08 ~ 5.67) *	2.73 (1.07 ~ 6.96) *	4.37 (1.94 ~ 9.88) ***
DMS	1.88 (0.96 ~ 3.69)	1.81 (0.71 ~ 4.60)	2.26 (0.83 ~ 6.12)	1.61 (0.60 ~ 4.26)
EMA	1.79 (0.79 ~ 4.07)	2.07 (0.80 ~ 5.33)	0.78 (0.21 ~ 2.90)	1.82 (0.67 ~ 4.96)

Note: The model was adjusted for all three insomnia symptoms, demographic variables (age, gender), and clinical covariates (illness duration, PANSS factor scores, antipsychotic dosage, clozapine use, polypharmacy, and sleep medication usage). ***: p<0.001; **: p<0.01; *: p<0.05. Counts: verbal aggression n=153, aggression against property n=52, auto-aggression n=33, physical aggression n=50.
Abbreviations: AOR, Adjusted Odds Ratio; CI, Confidence Interval; DIS, difficult initialing sleep; DMS, difficult maintaining sleep; EMA, early morning awakening.

all measured domains of aggression, from verbal to physical. Notably, neither difficulty maintaining sleep nor early morning awakening showed a significant independent association with aggression. These results challenge the conventional approach of treating insomnia as a monolithic entity and suggest that targeted assessment and treatment of difficulty initiating sleep may be a critical strategy for mitigating aggression in this vulnerable population.

Our study found that 14.6% of patients with chronic, stable schizophrenia exhibited clinically significant aggression. This rate is consistent with prior research in community-dwelling patients with schizophrenia,[4–6] but was much lower compared to the newly hospitalized sample (50.86%).[38] Patients with aggression demonstrated significantly worse psychiatric symptoms, particularly positive and excitement symptoms. These findings collectively underscore that aggression remains a significant clinical issue even in chronic, treated populations and is associated with a more severe psychopathological profile, highlighting the need for routine aggression risk assessment throughout all phases of the illness.

The current study demonstrates a robust link between insomnia and aggression among chronic inpatients with schizophrenia, which is in line with previous discoveries in different clinical contexts.[4,6,16] This aligns with a broader body of evidence, much of it from our own team, demonstrating that insomnia is closely related to numerous negative outcomes in schizophrenia.[7–13] Altogether, these results strengthen the clinical significance of regarding insomnia not just as a secondary symptom, but as a crucial modifiable risk factor for unfavorable outcomes in schizophrenia. Consequently, screening for and treating insomnia is of great significance in the case of schizophrenia.

Our study provides a novel contribution by being the first to specifically dissect the relationship between individual insomnia symptom profiles and aggression, demonstrating the specific and independent association between DIS and aggression. A potential explanation for this unique link lies in the psychophysiological hyperarousal model of insomnia.[24] From a cognitive perspective, the pre-sleep period for individuals with DIS is often characterized by cognitive and physiological hyperarousal, including rumination. This state of sustained, repetitive negative thinking can amplify negative affect and has been directly linked to increased anger and aggression.[39] Neurobiologically, this hyperarousal may impair top-down regulation from the prefrontal cortex over limbic regions like the amygdala. This impairment can lead to heightened emotional reactivity, eroded self-control, and a hostile cognitive bias before sleep even begins.[20,21,40] This process can create a vicious cycle: the stress of being unable to sleep degrades regulatory capacity, making daytime aggression more likely, and the arousal from that aggression then further disrupts the ability to initiate sleep the following night.[41] While all forms of sleep loss can lead to this impairment, the acute and frustrating experience of DIS may create a state of heightened arousal and emotional dysregulation that is more directly catalytic for an aggressive response compared to the states of fatigue that may follow DMS or EMA.

The study has several limitations. First, the cross-sectional design cannot establish causal inferences; it is impossible to determine whether DIS is a precursor to aggression or a consequence of the psychopathological state associated with it. Second, our assessment of insomnia relied on rating scales rather than objective measures like actigraphy or polysomnography, making the data susceptible to reporting biases. Furthermore, sleep duration and other comorbid primary sleep disorders (eg, sleep apnea or restless legs syndrome) were not measured. Third, our samples were composed of the chronic, well-treated, hospitalized inpatients. Individuals in earlier or untreated stages of illness often exhibit higher levels of insomnia and aggression. This specific environment, with its structured routines and constant

supervision, may modify the relationship between insomnia and aggression. Consequently, our findings may not be directly generalizable to outpatients or to individuals in earlier stages of the illness, such as first-episode cohorts, who often exhibit different clinical profiles and environmental stressors. Finally, we did not use a dedicated scale for depression, a significant comorbidity linked to both insomnia and aggression; however, we did account for mood symptoms using the validated PANSS mood factor which included the assessments of depressive symptoms. While we controlled for key variables, the possibility of residual confounding from unmeasured factors, such as genetic predispositions or recent life stressors, cannot be ruled out. Future research employing longitudinal designs with objective measures across diverse patient populations is warranted to corroborate these findings.

Conclusion

This study provides strong evidence that difficulty initiating sleep is a specific and independent factor associated with aggression among patients with chronic schizophrenia. This finding underscores the importance of detailed sleep assessment in clinical practice, moving beyond a generic diagnosis of insomnia to identify specific symptom profiles. Longitudinal and interventional studies are essential to confirm this association, establish causality, and formally test whether treatments targeting DIS can effectively mitigate aggressive behaviors.

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Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author Xiangyang Zhang.

Ethics Approval and Informed Consent

Written informed consent was obtained from all participants prior to enrollment. The Institutional Review Board of the Institute of Psychology, Chinese Academy of Sciences reviewed and approved the study (H18031).

Author Contributions

Xiangyang Zhang and Pu Peng contributed to the conceptualization, methodology, supervision, writing-original draft, Writing-review & editing, project administration. Lili Wei contributed to the methodology, investigation, Validation, visualization, writing-original draft. Yanan Zhou contributed to the investigation and writing-reviewing and editing. All authors agree to take responsibility and be accountable for the contents of the article. All authors gave final approval of the version to be published and agreed on the journal to which the article has been submitted.

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Disclosure

There are no relevant financial or non-financial competing interests to report.

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