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ORIGINAL RESEARCH

Factors Affecting Negative Symptoms in Schizophrenia and Their Relationship with Anxiety and Depression

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Objective: Negative symptoms significantly impair daily functioning and worsen clinical outcomes. Meanwhile, these symptoms are closely linked to anxiety and depression, further complicating prognosis. The mechanisms underlying these relationships remain unclear. This study aims to identify the factors influencing negative symptoms in schizophrenia and examine their relationship with anxiety and depression to guide more effective interventions and improve patient outcomes.

Methods: This study recruited 300 inpatients with schizophrenia from October 2022 to May 2023. Sociodemographic data and clinical characteristics were collected via a self-designed questionnaire. Negative symptoms, depression, and anxiety were assessed using the SANS, HAMD, and HAMA scales, respectively.

Results: Multiple regression analysis indicated that familial support ($\beta = -1.285$, $P = 0.005$), friend support ($\beta = -0.797$, $P = 0.032$), sleep quality ($\beta = 2.307$, $P < 0.001$), anxiety ($\beta = 0.264$, $P = 0.004$), and depression ($\beta = 0.324$, $P = 0.007$) were the main factors influencing negative symptoms. After adjusting for the duration of psychiatric disorder and type of antipsychotic medication as covariates, the above factors remained primary contributors to negative symptoms.

Conclusion: Enhancing familial support, friend support, and addressing emotional health and sleep disturbances are strategies that may alleviate negative symptoms in patients with schizophrenia.

Keywords: negative symptoms, anxiety, depression, schizophrenia, mental health

Introduction

Schizophrenia is a complex psychiatric disorder, psychosis symptoms include positive symptoms such as hallucinations and delusions, cognitive dysfunction in memory and executive function, and negative symptoms such as avolition, aphasia and affective blunting.[1–3] Negative symptoms can be further divided into experiential (eg, avolition, asociality, anhedonia) and expressive (eg, alogia, affective blunting) dimensions, which are considered core features of schizophrenia.[4] Studies have shown that more than 50% of patients with schizophrenia present with at least one negative symptom, and these symptoms are predominant in up to 60% of patients.[5–7] Even after the stabilization of psychotic symptoms, individuals with schizophrenia still experience negative symptoms. For example, Ander Heiden et al reported that 50% of first-episode schizophrenia patients still had residual negative symptoms five years after remission.[8] Negative

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symptoms are closely associated with poor clinical outcomes, including low treatment response rate, poor daily functioning, metabolic syndrome related symptoms, which seriously affect the quality of life and impose a heavy burden on the family and society.[1,6] Additionally, literature highlights that negative symptoms significantly impact patients' functional outcomes, including re-employment capabilities, instrumental role performance, and neurocognitive and independent functioning.[9] As negative symptoms worsen, cognitive function declines, and patients' sensitivity to reward diminishes, which could be one of the mechanisms through which negative symptoms impair functional outcomes.[10]

Patients with schizophrenia often experience anxiety and depression, and there is a complex interrelationship between negative symptoms and these anxiety and depression symptoms. And it has been suggested that depression and anxiety comorbid with schizophrenia are associated with a worse prognosis.[11,12] Studies have shown that negative symptoms, such as social withdrawal and anhedonia, not only reduce patients' social participation and life satisfaction, but may also increase the occurrence of anxiety and depressive symptoms.[8,13,14] The occurrence or exacerbation of anxiety and depressive symptoms may in turn exacerbate negative symptoms, creating a vicious cycle. However, some studies present contrary views, suggesting that depression comorbid with negative symptoms may indicate a better disease trajectory.[15] The relationship between negative symptoms of schizophrenia and anxiety symptoms remains unclear, and there is still some controversy regarding the connection between negative symptoms and anxiety and depression.[12,16,17]

To more comprehensively understand the impact of schizophrenia, this study aims to investigate the influencing factors of negative symptoms in patients with schizophrenia and to explore the relationship between negative symptoms and anxiety and depression. By deepening our understanding of these symptom interactions, we aim to develop reliable clinical outcome assessment tools that can guide the development of more effective treatment strategies. These strategies are expected to target mental symptoms and improve the overall quality of life for patients with schizophrenia, ultimately supporting more personalized and impactful therapeutic interventions.

Materials and Methods

Study Design and Participants

A consecutive sampling strategy was used to recruit 300 inpatients with schizophrenia between October 2022 and May 2023. Inclusion criteria were 1) age ≥18 years; 2) diagnosis of schizophrenia according to ICD-11 criteria; 3) patient's hospitalization duration ≥6 months; 4) ability to understand the literal meaning of the scales and to give a response; and 5) basic communication skills and consent to participate in this study. Exclusion criteria included poor adherence or inability to cooperate in completing the questionnaire, ie, inability to maintain attention and sustained participation in the dialogue during communication, or a record of multiple refusals of treatment as reported by the primary nurse. All participants gave informed consent to participate in this study.

Sample Size

To ensure the accuracy and reliability of the results, the sample size of this study was calculated using 10 events per variable, and there were 15 variables used in this study, with a preliminary estimate of 150 cases needed, plus 15% invalid variables, resulting in a final estimate of 173 samples needed. A total of 300 subjects were included in this study, all of whom met the inclusion and exclusion criteria.

Questionnaire

General Information

A self-designed questionnaire was utilized to obtain socio-demographic data and clinical characteristics, eg gender, age, education background, religious beliefs, pre-hospitalization employment status, medical staff support, familial support, friend support, sleep quality, exercise frequency, duration of psychiatric disorder and type of antipsychotic. In this study, religious beliefs were categorized into a binary variable: "never" and "yes", and this information was directly obtained from the patients or their relatives. The levels of medical staff support, familial support, and friend support were assessed using self-reported measures on a 0 to 100-point scale. The scale was divided into five levels: 1. Very large (81–100 points), 2. Large (61–80 points), 3. Moderate (41–60 points), 4. Small (21–40 points), and 5. Very small (0–20 points).

Medical staff support included assistance with managing emotional and psychological issues, providing continuity of care, and offering social concern. Familial support referred to emotional help and assistance with decision-making. Friend support was assessed by determining whether patients could rely on their friends for help during difficult times and for sharing their feelings. Sleep quality was rated based on the patient's recent sleep status, using the same 0 to 100-point grading scale. Additionally, the Hamilton Rating Scale for Depression (HAMD), the Hamilton Anxiety Scale (HAMA), and the Scale for Assessment of Negative Symptoms (SANS) were among the assessment tools employed.

Scale For Assessment Of Negative Symptoms

Scale for Assessment of Negative Symptoms, introduced in 1982 by American scholar N. Andreasen, is a tool utilized to measure the negative symptoms exhibited by patients with schizophrenia.[18] It consists of 25 items and is organized into five distinct subscales: affective flattening or blunting, alogia, avolition-apathy, anhedonia-asociality, and attention. Each subscale is rated on a scale from 0 (indicating no symptoms) to 4 (signifying very severe symptoms), with higher scores reflecting a more severe symptom profile.[19]

Hamilton Depression Scale

The Hamilton Depression Scale, introduced by Hamilton in 1960, is primarily utilized in clinical settings to assess a person's melancholy state by examining their current circumstances or those experienced over the course of a week.[20] This scale, widely employed in Psychiatry, is available in three versions: 17, 21, and 24 questions, with the latter utilized in this study.[21] It encompasses various factors such as affective state, interests, mental and physical anxiety, somatic symptoms, sleep difficulties, and suicidal ideation, with a maximum score of 76. Specifically, a rating above 35 denotes severe depression, a score between 21 and 35 indicates a depressive diagnosis, a score between 8 and 20 suggests depressive tendencies, and a score below 8 implies the absence of depressive symptoms.

Hamilton Anxiety Scale

The Hamilton Anxiety Scale, created by Hamilton in 1959, is one of the most widely used and renowned instruments in psychiatric clinics.[22] The 14-item scale effectively captures symptoms of anxiety, dividing them into two primary categories: somatic and neurotic anxiety. It is primarily evaluated on a 5-point scale, ranging from 0 (no symptoms) to 4 (severe symptoms), providing a nuanced understanding of the severity of anxiety symptoms. The total score on the HAMA scale offers valuable insights into the intensity of a patient's anxiety symptoms. Specifically, a total score exceeding 29, 21, 14 indicates severe, obvious, or certain anxiety, respectively.[19]

Data Collection Procedure

A team of five experienced nurses who underwent standardized training conducted interviews and administered the questionnaires. Considering that the study subjects were patients with schizophrenia, and their cognitive abilities and mental states might affect the accuracy of their responses, the involvement of the primary nurses for verification was introduced. Initially, the patients independently completed the questionnaires. Subsequently, the primary nurses, based on their daily care observations and the patients' behaviors, independently assessed the patients' conditions and cross-checked the self-reported answers. During the verification process, the nurses did not directly alter the patients' responses but engaged in discussions with the patients to clarify answers, ensuring the highest possible accuracy. A total of 315 questionnaires were distributed, with 300 completed, resulting in a completion rate of 95.2%. Analysis of the 15 incomplete responses revealed that four patients withdrew after consenting but prior to the survey commencement, nine opted out during the process, and two refused further participation post-completion due to concerns over information leakage. This study adheres to the EQUATOR (STROBE) checklist.[23]

Ethical Statement

This study obtained ethical approval from the IRB of the Affiliated Brain Hospital of Guangzhou Medical University (approval number: 2023034, April 24, 2023). Written informed consent was obtained from all participants before inclusion. The entire study was carried out in accordance with the Declaration of Helsinki.[24]

Bias

The design, execution, and reporting of this study adhered to the STROBE checklist. However, there were the following deviations from the STROBE checklist during the study process: 1. Sample Size Calculation: The sample size for this study was empirically estimated based on 10 events per variable, rather than being determined through a detailed power analysis or effect size calculation. 2. Data Collection Procedure: The data collection process included verification by primary nurses. Although the nurses did not modify the patients' responses during the verification process, this step may have introduced some observational bias. Despite these deviations, the overall study still meets most of the STROBE checklist requirements, ensuring a certain level of scientific validity and transparency in the results.

Statistical Analysis

SPSS version 25.0 was used to analyze the data. Descriptive statistics were performed to analyze the socio-demographic and clinical characteristics of the patients. For continuous variables, the mean ± standard deviation was reported if they followed a normal distribution; if not, the median and interquartile range were used. To assess the differences in the severity of negative symptoms across various socio-demographic and clinical characteristics, these characteristics were categorized for comparison. For continuous variables that followed a normal distribution, independent samples *t*-tests or one-way ANOVA were used; for non-normally distributed continuous variables, the Mann–Whitney *U*-test or Wilcoxon signed rank test was employed. In addition, Pearson correlation analysis was conducted to explore the relationship between negative symptoms, depression, and anxiety in patients with schizophrenia. Subsequently, multiple linear regression analysis was performed, with the total SANS score as the dependent variable. Independent variables included socio-demographic and clinical factors that were statistically significant, as well as variables identified through Pearson correlation analysis. A two-tailed P-value of less than 0.05 was considered statistically significant.

Results

General Information of Participants

A total of 300 patients with schizophrenia were included in this study, with a mean age of 58.64 years (range: 18 to 88 years). The majority of patients were male (61.67%) and most had no religious affiliation (91.33%). Prior to hospitalization, 81% of the patients were either unemployed or retired, and 74.34% had received a middle school or high school education. Approximately 59.34% of the patients reported having strong familial support, while 64.66% had strong support from medical staff. However, only 17.33% of the patients reported receiving strong support from friends. In addition, 32.34% of the patients reported having general or poor sleep quality, and 46.67% did not engage in any weekly exercise. Regarding the duration of schizophrenia, 40.67% of the patients had been diagnosed with schizophrenia for 21–35 years, and 36.67% had been diagnosed for 36 years or more. The vast majority of patients (93.33%) were taking atypical antipsychotics. Detailed information is provided in Table 1.

The Relationship Between Demographic Factors and Negative Symptoms in Inpatients with Schizophrenia

As shown in Figure 1 there are significant differences in negative symptom scores among schizophrenia patients based on gender, religious belief, levels of familial support, friends support, sleep quality, and weekly exercise frequency. Specifically, the negative symptom scores of male patients were lower than those of female patients (38.33 ± 9.06 vs 40.39 ± 8.31, p=0.044), suggesting that gender may play a role in the manifestation of negative symptoms, albeit with a small difference (Figure 1a). Patients without religious beliefs had significantly higher negative symptom scores compared to those with religious beliefs (39.47 ± 8.88 vs 35.46 ± 7.38, p=0.014), indicating that religious beliefs may provide some psychological support to patients, thereby alleviating negative symptoms (Figure 1d). Both family support (P = 0.015) and friend support (P = 0.004) showed a significant impact on negative symptoms. Patients with strong family support had lower negative symptom scores (eg, patients with "very large" family support had SANS scores of 39.04 ± 9.94), while those with insufficient friend support had more severe negative symptoms (eg, patients with "very small" friend support had SANS scores of 40.17 ± 9.64), suggesting that social support may play a role in alleviating

Table 1 General Information of Inpatients with Schizophrenia

Item	Frequency	Proportion (%)
Gender		
Female	115	38.33
Male	185	61.67
Age (Years old)		
18~35	15	5.00
36~53	62	20.67
54~71	184	61.33
72~88	39	13.00
Educational background		
Elementary or less	31	10.33
Middle school	107	35.67
High school	116	38.67
University and above	46	15.33
Religious beliefs		
Never	274	91.33
Yes	26	8.67
Pre-hospitalization employment status		
Employed	47	15.67
Unemployed	140	46.67
Self–employed	5	1.67
Retired	103	34.33
Other	5	1.67
Medical staff support		
Very small	1	0.33
Small	5	1.67
Moderate	100	33.33
Large	124	41.33
Very large	70	23.33
Familial support		
Very small	18	6.00
Small	23	7.67
Moderate	81	27.00
Large	128	42.67
Very large	50	16.67

(*Continued*)

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Table 1 (Continued).

Item	Frequency	Proportion (%)
Friend support		
Very small	143	47.67
Small	47	15.67
Moderate	58	19.33
Large	43	14.33
Very large	9	3.00
Sleep quality		
Very good	58	19.33
Good	145	48.33
General	86	28.67
Poor	11	3.67
Very poor	0	0.00
Exercise frequency (Weeks)		
0	140	46.67
1~2	74	24.67
3~4	38	12.67
>4	48	16.00
Duration of psychiatric disorder (Years)		
≤20	68	22.67
21–35	122	40.67
≥36	110	36.67
Type of antipsychotics		
Typical	10	3.33
Atypical	280	93.33
Combination	10	3.33

negative symptoms (Figure 1g and 1h). Patients with poorer sleep quality (eg, patients rated as having "poor" sleep had SANS scores of 46.91 ± 9.12) exhibited more severe negative symptoms (Figure 1i). Patients who exercised more than four times per week had significantly lower negative symptom scores (35.82 ± 8.07) compared to those who exercised less frequently, suggesting that exercise may have a positive effect on improving negative symptoms in schizophrenia patients (Figure 1j). However, factors such as educational background, pre-hospitalization employment status, the level of medical staff support, and age stratification do not show statistically significant differences in negative symptom scores among inpatients with schizophrenia ($P > 0.05$).

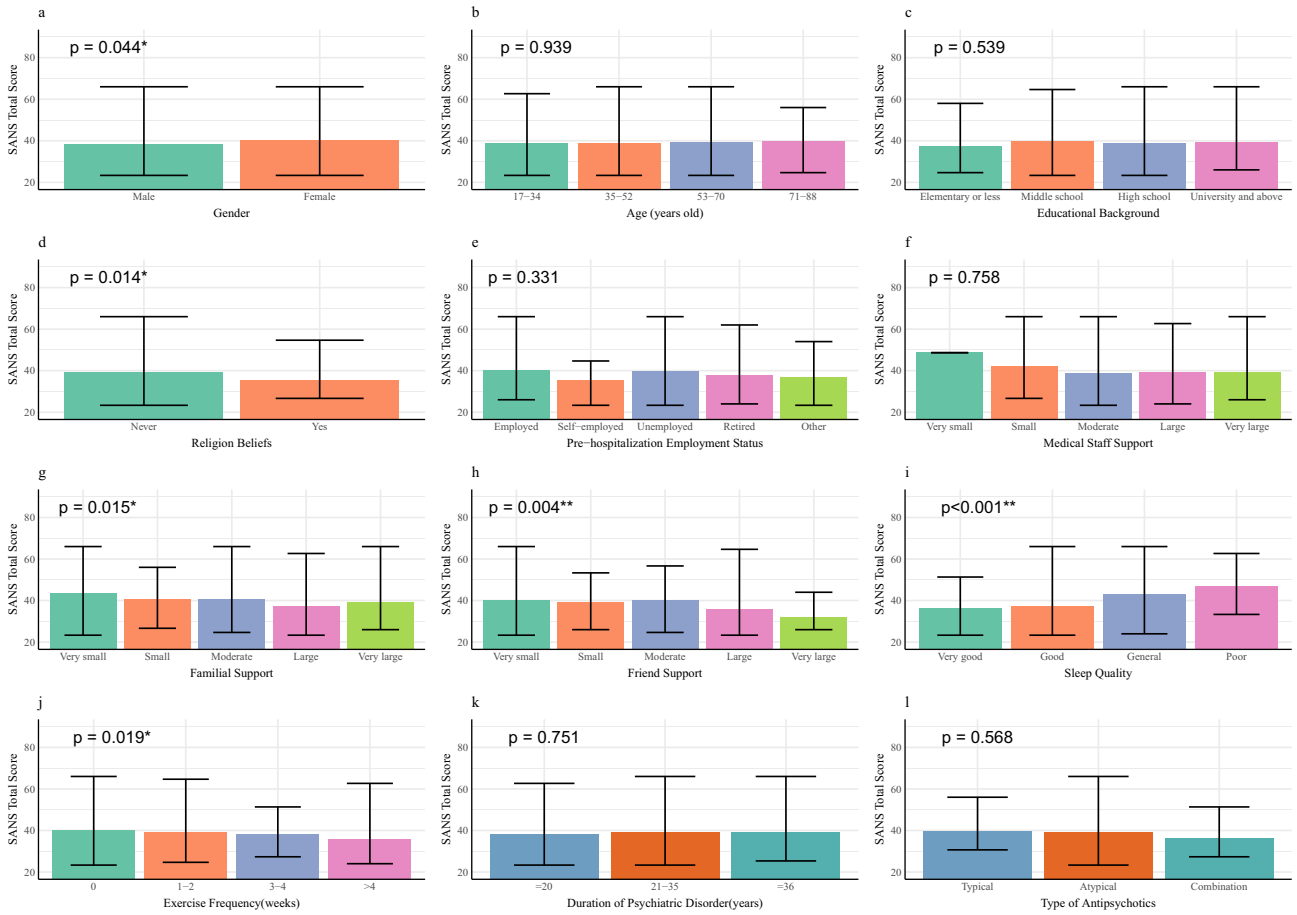

Figure 1 Comparison of Negative Symptom Severity Across Different Demographic and Clinical Characteristics in Inpatients with Schizophrenia. (**a**): Gender; (**b**): Age; (**c**): Educational background; (**d**): Religion beliefs; (**e**): Pre-hospitalization employment status; (**f**): Medical staff support; (**g**): Familial support; (**h**): Friends support; (**i**): Sleep quality; (**j**): Exercise frequency (weeks); (**k**): Duration of psychiatric disorder (years; (**l**): Type of antipsychotic.
Note: *P*<0.05=*, *P*<0.01=**.

Correlations Between Negative Symptoms, Depression, and Anxiety

As shown in Figure 2, the correlation coefficient between SANS and the HAMD was 0.39 ($P < 0.05$), and the correlation coefficient with the HAMA was 0.38 ($P < 0.05$). There was a moderate positive correlation between SANS scores and both HAMD and HAMA scores. This suggests that patients with higher levels of depression and anxiety are more likely to exhibit more severe negative symptoms.

Results of Linear Regression Analysis of the Negative Symptoms in Inpatients with Schizophrenia

As shown in Table 2, the results of the multiple linear regression analysis indicated that familial support, friends support, sleep quality, anxiety levels, and depression levels were significant predictors of negative symptoms ($P < 0.05$), collectively explaining 27.3% of the variance in negative symptom scores (adjusted $R^2 = 0.253$). Increased familial support and friends support were significantly associated with a reduction in negative symptoms ($P = 0.005$ and $P = 0.032$, respectively), while poorer sleep quality and higher levels of HAMA scores and HAMD scores were significantly associated with an increase in negative symptoms ($P < 0.01$). These results further suggest that providing social support, improving sleep quality, and addressing emotional health may play a key role in alleviating negative symptoms. Since this study focused on non-pharmacological factors, the Duration of psychiatric disorder and Type of antipsychotic were included as covariates to reduce confounding. The results still showed that familial support, friends support, sleep quality, HAMA scores, and HAMD scores remained significant predictors of negative symptoms ($P < 0.05$), as shown in Table 3.

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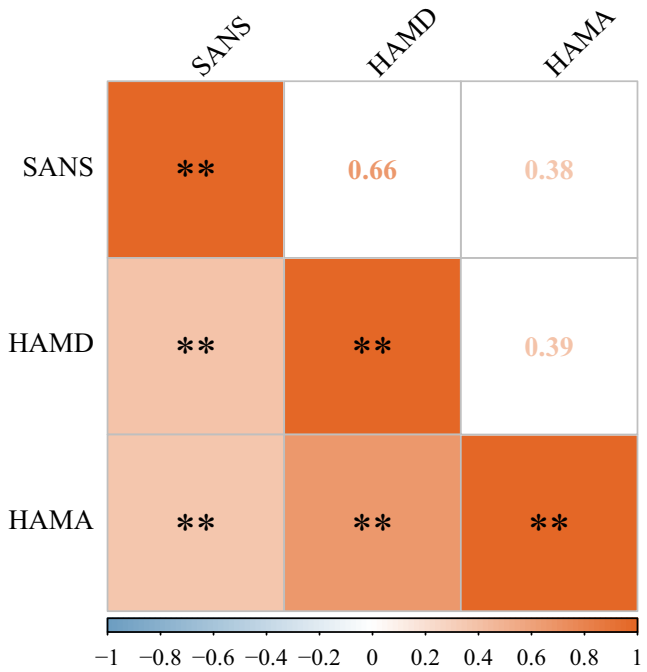

Figure 2 Correlation Between Negative Symptoms, Depression, and Anxiety in inpatients with Schizophrenia.
Note: *P*<0.05=*, *P*<0.01=**.
Abbreviations: SANS, Scale for Assessment of Negative Symptoms; HAMD, the Hamilton Depression Scale; HAMA, the Hamilton Anxiety Scale.

Discussion

There are two findings from this study. Firstly, the results of this study indicated that negative symptoms in patients with schizophrenia are related to family support, friend support and sleep quality. Secondly, negative symptoms in patients with schizophrenia are positively correlated with depression and anxiety.

Notably, the results of this study indicated that negative symptoms in patients with schizophrenia are related to family support and friend support. A previous study found that social support in patients with schizophrenia was a factor influencing negative symptoms, that is, lower social support could predict higher negative symptoms, which is in accordance with the results of this study.[25] Some scholars have suggested that greater spiritual and material support

Table 2 Linear Regression Analysis of Influencing Factors of Negative Symptoms in Inpatients with Schizophrenia

Item	Non-standardized Coefficient		β	t	P	VIF	95% CI
	β	Standard Error					
Gender	1.005	0.934	0.055	1.076	0.283	1.063	−0.833, 2.842
Religious beliefs	−1.343	1.651	−0.043	−0.813	0.417	1.113	−4.592, 1.907
Familial support	−1.285	0.454	−0.152	−2.832	0.005**	1.161	−2.178, −0.392
Friend support	−0.797	0.370	−0.111	−2.152	0.032*	1.065	−1.526, −0.068
Sleep quality	2.307	0.607	0.203	3.799	<0.001**	1.140	1.112, 3.503
Exercise frequency	−0.146	0.423	−0.018	−0.344	0.731	1.138	−0.978, 0.687
HAMA	0.264	0.091	0.197	2.901	0.004**	1.851	0.085, 0.442
HAMD	0.324	0.119	0.187	2.718	0.007**	1.903	0.090, 0.559

Notes: R2=0.273, Adj. R2=0.253, F=13.687, P=0.000; P<0.05=*, P<0.01=**.

Table 3 Linear Regression Analysis of Influencing Factors of Negative Symptoms in Inpatients with Schizophrenia, Adjusted for Duration of Psychiatric Disorder (Years) and Type of Antipsychotic

Item	Non-standardized Coefficient		β	t	Pa	VIF	95% CI
	β	Standard Error					
Gender	1.084	0.940	0.060	1.153	0.250	1.073	−0.767, 2.934
Religious beliefs	−1.264	1.657	−0.040	−0.763	0.446	1.117	−4.525, 1.998
Familial support	−1.309	0.456	−0.155	−2.869	0.004**	1.169	−2.207, −0.411
Friend support	−0.794	0.371	−0.111	−2.139	0.033*	1.066	−1.525, −0.063
Sleep quality	2.312	0.609	0.203	3.798	0.000**	1.141	1.114, 3.510
Exercise frequency	−0.162	0.425	−0.020	−0.382	0.703	1.143	−0.998, 0.674
HAMD	0.264	0.091	0.197	2.894	0.004**	1.852	0.084, 0.443
HAMA	0.331	0.120	0.191	2.759	0.006**	1.912	0.095, 0.567

Notes: R2=0.275, Adj. R2=0.250, F=10.981, P=0.000; P<0.05=*, P<0.01=**. a=adjusted for Type of antipsychotics and duration of psychiatric disorder (years) as covariates.

from one's environment equips individuals to face life's challenges better. Patients with schizophrenia, however, often experience limited external support due to cognitive impairments, the burdens faced by their families, and social stigma. Family and friend support can bolster patients' confidence, alleviate psychological pressure, and reduce negative symptoms, such as social withdrawal.[25–27] Thus, providing robust family and friend support is critical for these patients. Hospitals could consider offering long-term peer support groups and encouraging social volunteers to engage with patients, which may help reduce and improve negative symptoms.

Recently, one study also reported a similar result that there was a bidirectional relationship between sleep quality and the severity of mental symptoms. On the one hand, poor sleep quality indicated the deterioration of negative emotions and cognitive symptoms. On the other hand, severe mental symptoms indicated poor sleep quality.[28] This might be related to neurobiological functions of the brain among patients with schizophrenia. Reeve et al conducted a study that showed that sleep quality affected the neurobiological functions of the brain, especially in areas related to emotional regulation and cognitive function, which might lead to negative symptoms.[29] Aside from neurobiological functions, there is also another reason that schizophrenia is a disease that directly interferes with perception of reality, and patients are likely to experience distortions in their perception of time.[30] This finding suggests that sleep quality and negative symptoms in patients with schizophrenia interact with each other, and improving sleep quality might help improve negative symptoms. Therefore, the assessment, treatment, and management of sleep problems would be a major focus of attention for patients with schizophrenia. Taken together, family support, friend support and sleep quality could be vital for improvement of negative symptoms among patients with schizophrenia, which help psychiatrists evaluate therapeutic effect of schizophrenia as well.

Besides, the results of this study showed that negative symptoms are related to depression among patients with schizophrenia. Previous research has identified a non-reciprocal relationship, where higher levels of depression correspond to more severe negative symptoms, while more severe negative symptoms relate to lower depression.[14] However, this study only found a correlation between the two variables, which might be due to the milder severity of negative symptoms in the study subjects, no expression disorders, and limited ability to report depressive emotions. Gareth's psychological models of psychosis proposed that emotional changes directly influence psychiatric symptoms, suggesting that depressive emotions may drive the development of negative symptoms.[31] Depressive emotions might lead to social avoidance, causing patients to participate less in social activities and have fewer opportunities to interact with others, resulting in negative symptoms such as social withdrawal.[32] Furthermore, depressive emotions are often accompanied by an increase in self-attention and negative thinking. Therefore, a comprehensive intervention program combining social skills training and cognitive behavioral therapy can be developed to reduce depressive

symptoms from multiple angles and improve the treatment effect, thereby improving the negative symptoms of patients.

Additionally, this study showed that anxiety could affect negative symptoms in patients with schizophrenia. On one hand, anxiety can interfere with patients' attention and thought processes, making it more difficult for them to concentrate and handle daily tasks, thereby exacerbating negative symptoms such as lack of motivation and interest.[33] On the other hand, anxiety may also lead to social interaction difficulties for patients. Due to difficulties in maintaining focus and processing thoughts, patients may feel more anxious during social interactions, which inclines them to avoid social activities, creating a vicious cycle. This sense of isolation further intensifies negative symptoms.[34]

Overall, improving social support, sleep quality, depression, and anxiety are crucial for improving negative symptoms in patients with schizophrenia. These factors interact with each other and jointly affect the patient's recovery process. In addition, smoking may also be an important factor affecting negative symptoms.[35] Therefore, we must pay attention to these influencing factors, timely identification and effective intervention. By providing targeted support and care, we can help patients better manage these symptoms, thereby improving their overall condition.

Although a series of discoveries have been revealed in this study, limitations should be noted. Our research has some limitations and provides direction for future research. On the one hand, this study is a cross-sectional study. In the future, we hope to conduct multi-center, randomized controlled trials to explore negative symptoms of schizophrenia. On the other hand, the current research subjects are schizophrenia patients in Chinese hospitals. In the future, we hope to compare the differences in the influencing factors of negative symptoms in schizophrenia patients from different countries.

Conclusion

This study identifies significant factors influencing negative symptoms in patients with schizophrenia, such as familial and friends support, sleep quality, depression, and anxiety. Increased social support and better sleep quality are linked to fewer negative symptoms, while higher levels of depression and anxiety contribute to more severe symptoms. By targeting negative symptoms through comprehensive support and addressing emotional health and sleep disturbances, healthcare providers can improve the overall quality of life for schizophrenia patients. Ultimately, these efforts will support the development of more personalized and impactful therapeutic interventions.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

This study obtained ethical approval from the IRB of the Affiliated Brain Hospital, Guangzhou Medical University (approval number: 2020028). Written informed consent was obtained from all participants before inclusion. The entire study was carried out in accordance with the Declaration of Helsinki.

Consent for Publication

All patients in this study agree to publish.

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Disclosure

The authors report no conflicts of interest in this work.

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