

## **Effectiveness of a day treatment program for negative symptoms in patients with schizophrenia**

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### **Summary**

**Aim.** To evaluate the effectiveness of a day treatment program in reducing primary negative symptoms in people with schizophrenia and to identify predictors of treatment response.

**Material and methods.** This study was conducted at the Day Treatment and Rehabilitation Centre for people suffering from psychosis. Forty-three participants were assessed using PANSS, BNSS, CDSS, MOCA and FAB scales before and after 3 months of treatment. The therapeutic program included individual and group psychotherapy, social skills training, psychoeducation, music therapy, movement therapy, art therapy, occupational therapy, therapeutic community meetings, family sessions, and therapeutic excursions.

**Results.** Participants showed a significant decrease in negative symptoms and depressive symptoms following treatment. Improvement was observed in all five domains of negative symptoms. Regression analysis showed that intact motor programming skills were a significant predictor of improvement in negative symptoms. Improvement in insight correlated with better treatment outcomes.

**Conclusions.** The day treatment program was effective in treating primary negative symptoms in all five domains. Further research with a larger sample size and a control group is needed.

**Keywords:** negative symptoms, day treatment program, schizophrenia

## Introduction

Negative symptoms in schizophrenia represent the most stable of all symptom domains and have the worst impact on functioning in people with that disorder [1]. Nevertheless, studies have demonstrated that primary negative symptoms also fluctuate over time [2]. The most important clinical distinction of negative symptoms is between primary and secondary symptoms, where the former are a consequence of the psychopathology of schizophrenia and are experienced by almost 60% of patients [3]. Among the chief causes of secondary negative symptoms are depressive and positive psychotic symptoms [4].

Currently, the state-of-the-art conception of negative symptoms divides them into 5 individual domains: avolition, anhedonia, asociality, blunted affect and alogia [1]. To date, the gold standard of assessment is the clinician's examination of negative symptoms via clinical instruments, although recent studies have attempted to use experience sampling methods (ESMs) [5]. Recent expert guidelines in the field recommend the use of second-generation clinical tools, such as the Brief Negative Symptoms Scale (BNSS) and Clinical Assessment Interview for Negative Symptoms (CAINS) [6]. First-generation scales such as PANSS and SANS can lead to low measurement accuracy. This is primarily because both scales rely extensively on the behavioral observations of the respondent; additionally, some content overlaps with functional measures, and they contain items that do not belong to the domain of negative symptoms [6]. Moreover, first-generation scales distinguish poorly between primary and secondary negative symptoms, whereas second-generation scales do much better in this respect. Primary negative symptoms are relatively difficult to treat, and pharmacological interventions have only moderate efficacy [7]. Among drugs, second-generation antipsychotics (SGAs) appear to be the most effective, with an average effect size of  $-0.58$  [8]. Nonpharmacological interventions that reduce the severity of negative symptoms include exercise interventions, music therapy, cognitive-behavioral therapy, social skills training, acceptance and mindfulness-based therapies, group therapies, cognitive remediation (CR) and family-based therapies. A recent meta-analysis of these studies concluded that most were of low or very low quality and generally of low or at most moderate effectiveness [9]. Moreover, negative symptoms were not a primary target of these interventions, whereas the PANSS was the most prevalent tool for the assessment of negative symptoms, followed by other first-generation scales. In partial opposition to these findings, a previous meta-analysis of CBT interventions for negative symptoms failed to show any of the positive effects that were initially reported in older studies involving this therapeutic modality [10]. The EPA does not recommend any specific treatments for primary negative symptoms—only emphasizing that there is a need to provide access to rehabilitation interventions, such as supported employment or assisted housing [7]. Furthermore, the paper states that, if based solely on these few studies, recommendations for psychiatric rehabilitation should receive a grade of D. Ultimately, the grade was raised to a B, with the knowledge and experience of the guideline authors. Similarly, the Polish guidelines underscore the importance of implementing additional auxiliary psychosocial support programs [11]. One such complex

intervention is day hospital, which enjoyed a period of popularity in the early 2000s across numerous European countries [12]. The term ‘day hospital’ encompasses units that may perform slightly different functions. These include a day treatment center, which represents a form of intensified outpatient treatment; a transitional day hospital, which serves to bridge the gap between inpatient and outpatient treatment; and a day care center for patients requiring long-term care [13].

In the past two decades, a limited number of studies have been conducted to examine the efficacy of day hospitals in treating psychotic patients and their results are inconclusive [14,15]. Little is known about the moderators of the effectiveness of nonpharmacological therapeutic interventions. A meta-analysis of CBT interventions for schizophrenia, which investigated possible treatment moderators for negative symptoms, revealed no significant moderators [16]. Similarly, in the case of cognitive remediation, which has some of the best evidence for the treatment of negative symptoms, there is a lack of knowledge about moderators and mediators of treatment efficacy. One possible mediator of treatment effectiveness could be an improvement in insight. In one study, primary negative symptoms were found to be associated with lower levels of insight [17]. In another study, having better insight was a predictor of improvement in positive and negative psychotic symptoms [18]. In general, a relatively large number of studies have reported a negative correlation between insight and negative symptoms, suggesting that both negative symptoms and a lack of insight may be the result of hypofrontality [19].

A final aspect regarding the effectiveness of negative symptom treatment is its specificity. For example, CBT improves only avolition, anhedonia and asociality (experiential negative symptoms), whereas cognitive remediation (CR) is effective only for blunted affect and alogia (expressive negative symptoms) [20].

The first aim of our study was to evaluate the effectiveness of a day treatment program on primary negative symptoms in people with schizophrenia and to determine its impact on different symptom domains. To control for the confounding effects of the two most important factors associated with secondary negative symptoms, we additionally measured positive psychotic and depressive symptoms. The second aim of the study was to identify potential patient-related factors that could influence treatment effects, i.e., clinical predictors and factors that could mediate changes in negative symptoms.

## Material

The study was conducted at the Day Treatment and Rehabilitation Center for individuals with psychosis at the Child, Adolescent and Adults Psychiatry Clinic in Krakow. The center runs two programs: an intensive psychotherapeutic program for post-inpatient treatment or as an alternative to hospitalization, and a rehabilitation-focused program aimed at improving social functioning despite persistent symptoms. Inclusion criteria were an ICD-10 diagnosis of schizophrenia or schizoaffective disorder (F20, F25) and age 18-60 years. Exclusion criteria included a concurrent diagnosis of addiction or serious somatic disorders with cognitive components. Of 108 people admitted, 83 were prequalified based on these criteria. Sixty-one subjects consented

to participate and completed initial tests, with 43 completing the second assessment. Among the 18 without second measurements, 6 had missing data, 2 were discharged early, 1 was referred for inpatient care, and 9 requested discharge against medical advice. All participants provided written informed consent. The study was approved by the Jagiellonian University Medical College Bioethics Committee and conducted in accordance with the Declaration of Helsinki. The first measurement occurred within 2 weeks of admission, and the second within 2 weeks before completion of the approximately 3-month treatment. For olanzapine dose equivalents, we used the defined daily dose method based on Leucht et al. [21]. The therapeutic program, developed over decades as part of Krakow's community treatment approach for schizophrenia emphasizes group activities based on therapeutic community principles [22]. Treatment focuses on developing insight, building treatment motivation, and improving social relationship skills. Interventions were provided with the weekly schedule and included individual and group psychotherapy (integrative approach), social skills training, psychoeducation, various therapies (music, movement, art, occupational), therapeutic community sessions, family meetings, and patient excursions. Except for individual psychotherapy and psychiatric consultations, all activities were group-based.

## Methods

The clinical instruments used in the study included the following:

- The Positive and Negative Syndrome Scale (PANSS) consists of 30 symptoms whose severity is measured on a scale from 1-7 [23]. The results were analyzed on the basis of the five-factor model [24], which distinguishes the positive, negative, excitement, disorganization and emotional symptoms domains. Additionally, we used the G12 item score – lack of judgment and insight – which is a simple but valid and relatively common tool used in studies to assess patient insight [25,26].
- The Brief Negative Symptom Scale (BNSS) measures 13 symptoms with severity measured on a scale from 0 to 6, which are divided into six subscales, i.e., blunted affect, alogia, asociality, anhedonia, avolition, and lack of distress [27].
- The Calgary Depression Scale for Schizophrenia (CDSS) consists of nine depression symptoms whose severity is measured on a scale from 0 to 3, yielding a single total score [28]. Depression was defined as a total CDSS score  $\geq 6$ , which represents an established cut-off point for clinically significant depressive symptoms in patients with schizophrenia, demonstrating high sensitivity (88%) and specificity (88%) for detecting depression in this population [29].
- The Montreal Cognitive Assessment (MoCA) is a screening tool for measuring global cognitive functioning. It allows the assessment of visuospatial and executive functions, language, attention, memory and verbal fluency [30]. It is a sensitive tool detecting cognitive impairment in schizophrenia patients [31].

- The Frontal Assessment Battery (FAB) is a short bedside cognitive and behavioral battery designed to assess frontal lobe functions [32]. It consists of six subtests. In our study, we used only three subscales: motor programming/Luria motor series, sensitivity to interference and inhibitory control. Each item has a score ranging from 0 to 3, with the lowest score corresponding to the highest frontal dysfunction.

Statistical analyses were performed using SPSS ver. 28. The normality of the distribution of the data was tested using the Shapiro–Wilk test. Since the normal distribution criterion was not met for a majority of the quantitative variables, comparisons before and after the treatment were conducted using the Wilcoxon test. The effect sizes were calculated as the z statistic divided by the square root of the sample size [33]. Correlations were calculated using Spearman’s rank correlation test. Multiple linear regression was performed to determine which variables were predictors of improvement in negative symptoms. All the analyses were performed on 43 participants with no missing data. The level of statistical significance was set at  $\alpha=0.05$ .

## Results

Data analysis was conducted on 43 participants, 44.2% of whom were female. The participants’ age ranged from 20 to 56 years, with a mean of 32.4 years. The mean duration of patients’ illness was 10.14 years, and the average number of inpatient psychiatric hospitalizations was 2.72. The participants were taking mostly (76.7%) atypical antipsychotics, with 23.3% taking first-generation antipsychotics. Approximately half of the participants were receiving antipsychotic monotherapy (46.5%) or polytherapy (53.5%). Almost all the participants had a diagnosis of schizophrenia (93.0%), with three people (7.0%) diagnosed with schizoaffective disorder. The demographic data are summarized in Table 1.

Table 1. Demographic and clinical characteristics of patients (N=43)

Characteristic	N (%) / M (SD)
Demographics	
Age (years)	32.4 (7.98)
Sex	
Female	19 (44.2)
Male	24 (55.8)
Marital status	
Married	6 (14.0)
Single	35 (81.4)
Divorced	2 (4.7)
Education level	

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Primary	2 (4.7)
Vocational	3 (7.0)
Secondary	20 (46.5)
Post-secondary	12 (27.9)
University	14 (32.6)
Clinical characteristics	
Diagnosis	
Schizophrenia	40 (93.0)
Paranoid schizophrenia (F20.0)	34 (79.1)
Undifferentiated schizophrenia (F20.3)	2 (4.7)
Simple schizophrenia (F20.6)	2 (4.7)
Post-schizophrenic depression (F20.4)	2 (4.7)
Schizoaffective disorder	3 (7.0)
Duration of illness (years)	10.14 (7.79)
Number of hospitalizations	2.72 (2.66)
Comorbid depression (CDSS $\geq 6$ )*	20 (46.5)
Pharmacotherapy	
Antipsychotic generation	
First-generation: chlorprothixene, flupenthixol, haloperidol	10 (23.3)
Second-generation: amisulpride, aripiprazole, clozapine, quetiapine, olanzapine, risperidone	33 (76.7)
Antipsychotic therapy	
Monotherapy	20 (46.5)
Polytherapy	23 (53.5)
Olanzapine equivalent dose (mg)**	15.74 (12.32)
Antidepressant use	10 (23.3)

\*Depression defined as CDSS total score  $\geq 6$  [add reference]

\*\* For patients on multiple antipsychotics, equivalents were summed

Results of individual measurements before and after the intervention are presented in Table 2. Notably, the MOCA and FAB tests were only performed in the first measurement. A statistically significant decrease in the PANSS, BNSS and CDSS total scale scores was observed. A reduction in symptom severity was observed in all the subscales of the BNSS and in the PANSS negative and distress subscales. However, other results were not statistically significant. The effect sizes for all significant outcomes were small, with the exception of a moderate effect size for the total BNSS score. No significant difference was found in CDSS change scores between patients

taking antidepressant medication (n=10) and those not receiving such treatment (n=33) (U = 163.0, p = 0.942).

**Table 2. Baseline and posttreatment estimated means, medians and effect sizes for outcome measures**

Measure	Time	Mean	SD	Median	Min	Max	z	p	Effect size
BNSS total	pre	26.63	15.54	26.00	0.00	55.00	-3.462	0.004	0.53
	post	18.24	16.77	16.00	0.00	54.00			
BNSS anhedonia	pre	7.02	4.79	6.00	0.00	16.00	-2.879	0.009	0.44
	post	4.78	4.48	4.00	0.00	15.00			
BNSS distress	pre	1.46	1.34	1.00	0.00	5.00	-2.382	0.018	0.36
	post	0.83	1.02	1.00	0.00	4.00			
BNSS asociality	pre	4.34	2.79	4.00	0.00	10.00	-2.191	0.020	0.33
	post	3.07	3.04	2.00	0.00	10.00			
BNSS avolition	pre	4.61	3.18	5.00	0.00	10.00	-2.827	0.010	0.43
	post	3.07	3.13	2.00	0.00	10.00			
BNSS blunted affect	pre	6.24	4.73	6.00	0.00	14.00	-2.965	0.009	0.45
	post	4.37	4.60	3.00	0.00	14.00			
BNSS alogia	pre	2.95	2.72	2.00	0.00	11.00	-2.841	0.010	0.43
	post	2.12	2.88	1.00	0.00	11.00			
PANSS total	pre	57.67	19.62	53.00	30.00	128.00	-2.626	0.009	0.40
	post	51.60	17.11	50.00	30.00	88.00			
PANSS positive	pre	8.37	3.10	8.00	5.00	17.00	1.782	0.075	0.27
	post	7.66	2.56	7.00	5.00	13.00			
PANSS negative	pre	18.65	7.88	19.00	8.00	38.00	-2.282	0.022	0.35
	post	16.14	7.65	13.00	8.00	38.00			
PANSS excitement	pre	5.58	2.08	5.00	4.00	12.00	-1.444	0.149	0.22
	post	5.16	1.98	4.00	4.00	12.00			
PANSS distress	pre	9.14	4.11	8.00	5.00	23.00	-2.398	0.016	0.37
	post	7.91	3.32	6.00	5.00	17.00			
PANSS emotional	pre	8.09	4.20	7.00	4.00	23.00	-1.143	0.253	0.17
	post	7.37	3.03	7.00	4.00	14.00			

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Insight (G12)	pre	2.58	1.30	3.00	1.00	5.00	-1.492	0.136	0.23
	post	2.37	1.29	3.00	1.00	6.00			
CALGARY total	pre	5.12	5.19	3.00	0.00	23.00	-2.643	0.008	0.40
	post	3.41	3.32	3.00	0.00	12.00			

BNSS – Brief Negative Symptom Scale; PANSS – Positive and Negative Syndrome Scale; CALGARY – Calgary Depression Scale; SD – standard deviation; z – Wilcoxon test statistic; p – significance level

To identify potential predictors of treatment efficacy, a correlation matrix was constructed to examine the relationships between changes in the BNSS total score and the following variables: premeasurement of illness insight, antipsychotic dose, olanzapine equivalent, duration of illness, number of hospitalizations, MOCA score as a proxy of global cognitive function, MOCA verbal fluency and FAB subtests. Additionally, we added a CDSS change score, and insight change score and a PANSS positive change score to explore potential mediators or posttreatment moderators of outcome. The results are presented in Table 3.

Table 3. Correlation matrix between the change in the total BNSS score and the selected variables

Variable	Antipsychotic olanzapine dose equivalent (mg)	illness duration	Insight	Number of hospitalizations	BNSS baseline	FAB motor programming	FAB interference	FAB inhibitory	MOCA total	MOCA verbal fluency	Insight change	Calgary Depression Scale change	PANSS positive change
BNSS change	-0.252	-0.170	0.070	-0.158	0.293	0.363*	0.377*	-0.057	0.031	0.080	0.339*	0.193	0.272
p-level	0.102	0.283	0.657	0.313	0.056	0.017	0.013	0.717	0.845	0.612	0.026	0.215	0.078

BNSS – Brief Negative Symptom Scale; FAB – Frontal Assessment Battery; MOCA – Montreal Cognitive Assessment; CDSS – Calgary Depression Scale for Schizophrenia; PANSS – Positive and Negative Syndrome Scale; \*p < 0.05

Linear regression was performed to identify potential pretreatment or posttreatment predictors of improvement in negative symptoms. Changes in insight, FAB motor programming and FAB interference scores were chosen as independent variables, as all of them were significantly correlated with changes in the total BNSS score. Additionally, the baseline BNSS score was added to control for the baseline severity of negative symptoms. The scatterplot of standardized residuals versus standardized predicted values indicated that the data met the assumptions of linearity and homogeneity of residual variances. The residuals were approximately normally distributed (Shapiro–Wilk test, p=0.792). The residuals met the assumption of independence, as the Durbin–Watson value was 1.96. The VIFs of all the independent variables were close to 1. A significant relationship between the dependent variable and the baseline BNSS

score ( $p < 0.001$ ), insight change score ( $p = 0.002$ ), and FAB motor programming score ( $p = 0.029$ ) was established. The relationship between the postmeasure BNSS score, and FAB interference was not significant ( $p = 0.124$ ). There was a 5.76-point decrease in the postmeasure BNSS score for each extra point of increase in insight. For each point increase in the FAB motor programming score, there was a 4.24-point decrease in the postmeasure BNSS score, and for each point increase in the baseline BNSS score, there was a 0.82-point increase in the postmeasure BNSS score. The  $R^2$  value was 0.629, so 63% of the variation in the BNSS postmeasure score can be explained by the model consisting of the baseline BNSS, insight change, FAB interference and FAB motor programming. The results are summarized in Table 4.

Due to the small sample size, it was not possible to conduct a moderation or mediation analysis to test the role of insight change as a treatment mediator or FAB motor programming as a treatment moderator. For a simple mediation model to detect a medium effect size, the minimal sample size for the bootstrapping method is 80 [34].

Table 4. Results of linear regression for the change of total BNSS score as the dependent variable

Measure	B	SE B	$\beta$	t	95% CI	p	
			LL	UL			
Baseline total BNSS	0.816	0.113	0.737	7.219	0.587	1.045	<0.001
Insight change	-5.758	1.759	0.413	3.273	-9.320	-2.196	0.002
FAB interference	-2.881	1.831	0.200	1.573	-6.588	0.826	0.124
FAB motor programming	-4.238	1.862	0.293	2.276	-8.007	-0.469	0.029

BNSS – Brief Negative Symptom Scale; FAB – Frontal Assessment Battery; B – regression coefficient; SE B – standard error of coefficient;  $\beta$  – standardized regression coefficient; CI – confidence interval; LL – lower limit; UL – upper limit

## Discussion

The study demonstrated that comprehensive therapeutic intervention in the Day Treatment Centers resulted in a significant improvement in negative symptoms, as measured by both the BNSS and the PANSS, and depressive symptoms, as measured by the Calgary Depression Scale. However, no improvement was observed in the severity of positive symptoms as measured by the PANSS. The reduction in negative symptoms was significant for each of the five subscales, indicating that treatment in the day unit helps alleviate negative symptoms in all domains.

Few studies have evaluated the impact of day treatment program on negative symptoms. A Cochrane review has focused solely on the effect on overall symptoms, with no information on the effect on negative symptoms [13]. Another meta-analysis of community-based studies reported effects on overall symptoms but not on specific effects on negative symptoms [35]. Only a few papers have reported the results of studies utilizing similar interventions. In the study by Juretic et al. [14], no improve-

ment in negative symptoms was observed following the four-month intervention. However, a six-month follow-up period revealed the potential for improvement. This discrepancy between these results and our results may be attributed to the relatively lower intensity of the treatment program. A further multicenter study in Japan, which compared the treatment of schizophrenia patients in day care facilities with that of outpatients, demonstrated that there was no significant change in the severity of negative symptoms [15]. However, determining the average intensity of the intervention is challenging since the study included individuals who attended the facility one to five times a week for a period of four months. In another study conducted in a day care facility, after three years of treatment, no significant decrease in symptoms, as measured by the BPRS scale, was observed, including negative symptoms [37]. The authors attributed this to the relatively low severity of symptoms. The therapeutic program was relatively similar to our program, as it included group psychotherapy, social skills training, art therapy, occupational therapy and various group recreational activities. However, there was less emphasis on individual psychotherapy, which may also have contributed to the lack of significant improvement in negative symptoms. In another intervention [36], there was also no decrease in the severity of negative symptoms, as measured by the PANSS. Despite the intervention being intensive, with participants spending almost 8 hours daily in the ward, it is likely that the short duration of the intervention (5 weeks) was insufficient to result in an improvement in negative symptoms.

The difficulty in comparing our intervention to other behavioral and psychosocial interventions in reducing the severity of negative symptoms is dependent on the use of different measurement tools. In a recent meta-analysis of these types of interventions, more than 95% of the studies utilized the PANSS scale, a substantial proportion additionally utilized the SANS and BPRS scales, and a few utilized newer generation scales [9]. Additionally, most of them considered negative symptoms as a homogeneous concept, in part because the PANSS does not take into account the five-domain symptom division, unlike second-generation scales such as the BNSS. Moreover, on the basis of symptom network analyses, it appears that the five domains of negative symptoms constitute a relatively loose network [38], which implies that they are not to be treated as a single entity. Instead, five different symptoms with different neurobiological substrates should be considered. Therefore, it is unlikely that there is a one-size-fits-all treatment for negative symptoms and integrating various interventions could be necessary to reduce the symptoms in all domains. We did not conduct such an analysis in our study. Furthermore, it would be valuable in the future to examine the effects of day treatment program on the structure of the negative symptom network. Nevertheless, improvements in all symptom domains with similar effect sizes suggest that the comprehensive therapeutic program relies on different mechanisms of action for negative symptoms. Improvements in alogia and blunted affect seem especially important. In addition to our clinical experience that these two domains are particularly resistant to change, data from the literature indicate that alogia, flattened affect, and social withdrawal are the symptoms most specific to negative symptoms when they are differentiated from depressive symptoms [39].

A meta-analysis of psychosocial and behavioral interventions for negative symptoms in schizophrenia found that CR and exercise therapy produced greater effect sizes than other studied interventions [39]. Although our therapeutic program did not include these specific interventions, it nevertheless effectively reduced negative symptom severity. The possible explanation comes from the results of a systematic review with meta-analysis of group interventions in schizophrenia. It has been concluded that psychotherapeutic interventions were more effective for negative symptoms than standard treatment but showed similar effectiveness to active control groups, defined as nontherapeutic group meetings like support or discussion groups. It means, that treatment effectiveness correlated only with its intensity, not modality [40], suggesting that group interventions' efficacy largely stems from nonspecific group effects.

All patients were on stable antipsychotic treatment at the time of program initiation. The majority (76.7%) were taking second-generation antipsychotics, which show moderate efficacy in negative. However, the observed improvements were probably related to the therapeutic program for two reasons. First, the stability of pharmacological treatment before starting the program suggests that the therapeutic potential had already been utilized. Second, the systematic improvement across all five domains of negative symptoms, coupled with the lack of similar improvement in positive symptoms, suggests the influence of therapeutic mechanisms specific to the day treatment program rather than pharmacological effects, which typically show different patterns of efficacy.

The day treatment program also significantly reduced depressive symptom severity, with an effect size comparable to one observed for negative symptoms. This improvement likely occurred because several therapeutic activities in our program are also effective for treating depression. Literature supports this finding, as group sociotherapeutic interactions were effective in treating depression across various populations [41]. The lack of difference in CDSS improvement between patients with and without antidepressant medications indicates that the reduction in depressive symptoms was independent of antidepressant pharmacotherapy. Although the antidepressant properties of second-generation antipsychotics, used in the majority of patients, cannot be ruled out as a contributing factor, considering the stable pharmacotherapy prior to treatment initiation, the day treatment program appears to play a key therapeutic role. The lack of improvement in psychotic symptoms aligns with existing evidence; a meta-analysis showed that group interventions for schizophrenia significantly improved negative and general symptoms but not positive symptoms [40]. In our study, this lack of change in positive symptoms likely reflects that most patients had either already received treatment for acute positive symptoms in inpatient settings or had not experienced positive symptoms for months or years before admission.

Among the investigated treatment predictors, the majority appeared to have no significant association with improvement in negative symptoms. The only significant clinical predictor of treatment response tested in this study was the motor programming subscale of the FAB. The second FAB subscale, sensitivity to interference, which demonstrated a positive correlation with improvement in negative symptoms, was found to be nonsignificant in the linear regression model.

The Luria test, also referred to as the Fist-Edge-Palm (FEP) task, is a complex motor task designed to assess a specific subgroup of neurological soft signs (NSSs). NSSs may be both a trait factor related to genetic liability and a state factor that is an indicator of the severity of the disease process [42]. This is demonstrated by the observation that, in patients responding positively to treatment, the intensity of NSSs diminishes, whereas in treatment-resistant patients they persist or even increase. Furthermore, NSSs seem to serve as a marker for neurodevelopmental disorders, as they are more prevalent in patients with childhood – or adolescent-onset schizophrenia than in those with adult-onset schizophrenia [43]. In a study comparing individuals with schizophrenia and their first-degree relatives to healthy controls, Chan et al. [44] reported frontal dysfunction and a lack of functional connectivity between sensorimotor cortices and the right frontal gyrus in the former group when performing the FEP task. The authors of the study postulated that inferior FEP performance may represent one of the endophenotypes of schizophrenia, given that the prevalence of NSS increases progressively from healthy individuals through healthy relatives of individuals with schizophrenia to individuals with schizophrenia. It can thus be hypothesized that the subgroup of patients with an abnormal FEP score is characterized by a more severe disease course, with greater frontal lobe impairment and thus a poorer response to therapeutic interventions aimed at reducing negative symptoms. In other disease entities, the Luria test score may also serve as a marker of disease severity. In a study of individuals with dementia, an abnormal Luria test score was observed in the majority of patients with Alzheimer's disease or frontotemporal dementia, whereas only a minority of individuals with MCI and almost no healthy individuals presented with this finding [45].

The second (though not strictly clinical) predictor of treatment response, potentially mediating treatment effects, was improved insight. At this point, it is worth noting that according to the operationalization used, we refer to clinical insight, which encompasses the patient's awareness of their mental illness, recognition of symptoms, and understanding of the need for treatment. This differs from psychodynamic insight, which is defined as "the ability to perceive connections between one's own life history, i.e., the role of significant life events, personality traits, and family history, and the experience of mental illness [46]. This finding aligns with previous studies showing negative correlations between insight and negative symptom severity [19]. Longitudinal research indicates that insight improvement predicts negative symptom improvement [47]. While insight is a complex concept, operational models help explain its relationship with symptom improvement. The integrative model conceptualizes insight as emerging from the integration of information from internal states, external circumstances, and others' perspectives [26]. In schizophrenia, impaired self-reflection leads patients with poor insight to maintain premorbid self-images, incorrectly assuming their functioning remains unchanged from pre-illness states [48]. Additionally, lack of insight reduces treatment motivation [49]. Thus, patients with improved insight may more accurately assess their symptoms, developing greater willingness to change and treatment motivation. However, our results cannot exclude the possibility that insight improvement resulted from reduced negative symptom severity rather than causing it.

Interestingly, an earlier study in the same day unit found no correlation between insight changes and negative symptom improvement. The authors attributed this discrepancy to either the relatively short treatment duration averaging 11 weeks or the limited accuracy of the Brief Psychiatric Rating Scale (BPRS) for assessing negative symptoms [50]. Given our comparable intervention duration of 14 weeks, the second explanation seems more plausible. Our results demonstrate the day treatment program's positive therapeutic effect on primary negative symptoms. The absence of improvement in positive symptoms and the lack of association between improvements in depressive and negative symptoms suggest that two major causes of secondary negative symptoms were effectively excluded, though other potential secondary causes cannot be completely ruled out.

The main limitation of this study is the relatively small sample size, which may have affected the reliability of the findings. As a consequence, it was not feasible to perform a mediation or moderation analysis, thereby limiting the conclusions that can be drawn regarding the potential predictors of the treatment response. Additionally, the high attrition rate during the study period represents a further limitation. Our study did not include a control group. However, given the relative stability of negative symptoms over time, it only slightly reduces the certainty of findings. This is a common occurrence in the day unit setting due to the length of treatment and the necessity for regular attendance. Furthermore, the absence of a control group introduces a potential source of bias. While negative symptoms are generally stable over time, there is always the possibility of a change unrelated to treatment.

## Conclusions

Comprehensive therapeutic intervention in the day treatment program is moderately effective in alleviating primary negative symptoms in all five domains. A significant clinical predictor of improvement is a lack of dysfunction in executive functioning in motor planning. An improvement in insight was associated with better treatment outcomes. Further research with a larger sample size and a control group is needed to confirm the results and to clarify the role of potential predictors of treatment efficacy.

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