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Research Article

Effect of Yoga as an Add-On Therapy for Negative and Cognitive Symptoms in Patients with Schizophrenia—A Randomized Controlled Trial

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Abstract

Background: People with schizophrenia usually present with deficits of several neurocognitive domains—including attention, processing speed, working memory, verbal and visual memory, and executive function. Pharmacological treatment options are limited for both negative and cognitive symptoms. However, several non-pharmacological interventions, like yoga, have been tried with evidence of effectiveness in providing measurable cognitive gains and improving negative symptoms. ***Objective***: To find out the effect of yoga on negative and cognitive symptoms through a randomized controlled trial. ***Methods***: A single-blind randomized controlled trial was conducted at a tertiary care hospital from June 2023 to June 2025. Patients were screened with the PANSS scale, and scores <75 were included for the study. The sample size was calculated as 104. Two groups were formed with 60 participants in each group randomly: Group A, with patients who were given yoga intervention along with standard pharmacotherapy, and Group B, with patients who continued with the standard pharmacotherapy (olanzapine up to 30mg). Baseline PGIBBD and CTT scores were obtained from each participant at baseline and after the yoga intervention. ***Results***: After 3 months of intervention, Group A showed a marked and statistically significant reduction in symptom severity, with substantial improvements observed in both negative and cognitive symptom domains as measured by SANS scores, PGIBBD, and CTT scores. ***Conclusions***: The concurrent improvement in both symptom severity and cognitive measures in the yoga intervention group addresses not only clinical symptoms but also associated cognitive deficits, which are critical determinants of functional outcome.

Keywords: Cognitive deficit; Exercise; Negative symptoms; Psychosis; Yoga intervention.

تأثير اليوغا كعلاج إضافي للأعراض السلبية والمعرفية لدى مرضى الفصام — تجربة عشوائية محكمة

الخلاصة

الخلفية: عادة ما يظهر الأشخاص المصابون بالفصام بعجز في عدة مجالات عصبية معرفية—بما في ذلك الانتباه، سرعة المعالجة، الذاكرة العاملة، الذاكرة اللفظية والبصرية، والوظيفة التنفيذية. خيارات العلاج الدوائي محدودة لكل من الأعراض السلبية والمعرفية. ومع ذلك، تم تجربة عدة تدخلات غير دوائية، مثل اليوغا، مع أدلة على فعاليتها في توفير مكاسب معرفية قابلة للقياس وتحسين الأعراض السلبية. **الهدف**: معرفة تأثير اليوغا على الأعراض السلبية والإدراكية من خلال تجربة عشوائية محكمة. **الطرائق**: أجريت تجربة عشوائية محكمة أحادية التعمية في مستشفى رعاية ثالثية من يونيو 2023 إلى يونيو 2025. تم فحص المرضى باستخدام مقياس PANSS، وتم تضمين درجات <75 في الدراسة. تم حساب حجم العينة على أنه 104. تم تشكيل مجموعتين من 60 مشاركا في كل مجموعة بشكل عشوائي: المجموعة أ، مرضى تلقوا تدخل يوغا مع العلاج الدوائي القياسي، والمجموعة ب، مرضى استمروا في العلاج الدوائي القياسي (أولانزابين حتى 30 ملغ). تم الحصول على درجات PGIBBD وCTT الأساسية من كل مشارك في البداية وبعد تدخل اليوغا. **النتائج**: بعد 3 أشهر من التدخل، أظهرت المجموعة أ انخفاضا ملحوظا وذا دلالة إحصائيا في شدة الأعراض، مع تحسن ملحوظ في كل من مجالات الأعراض السلبية والمعرفية كما تم قياسها بدرجات SANS وPGIBBD وCTT. **الاستنتاجات**: التحسن المتزامن في شدة الأعراض والمقاييس الإدراكية في مجموعة التدخل اليوجي يعالج ليس فقط الأعراض السريرية بل أيضا العجز المعرفي المرتبط، الذي يعد من العوامل الحاسمة للنتائج الوظيفية.

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INTRODUCTION

Positive, negative, and cognitive symptoms are considered to be core symptoms of schizophrenia [1]. Negative symptoms are defined by five key features, i.e., diminished emotional expression (blunted affect), reduced speech output (alogia), lack of motivation (avolition), social withdrawal (asociality), and decreased ability to experience pleasure (anhedonia). Currently existing pharmacological treatments show only modest effectiveness in alleviating the negative symptoms of schizophrenia [2]. Furthermore, it is well recognized that a relapsing and remitting course has been observed in the majority of these patients [3]. People living with schizophrenia usually present with deficits across several neurocognitive domains,

including attention, processing speed, working memory, verbal and visual memory, and executive function [4]. Impairments in neurocognitive performance undermine functional capacity and community functioning. It also negatively impacts work success, independent living, and real-world outcomes, with internalized stigma acting as a contributing mediating factor [5]. Cognitive impairment also keeps away engagement of the user with mental health professionals, and that leads to limitations of recovery in the context of psychiatric rehabilitation [6]. There is a general consensus from various endophenotype studies that cognitive impairments in schizophrenia are often present before the emergence of psychotic symptoms, are also present during the acute psychotic episode, and persist even after remission of the psychotic symptoms [7]. Pharmacological treatment options are somewhat limited for cognitive symptoms. However, several non-pharmacological interventions have been tried, and there is varying evidence of their effectiveness in providing measurable cognitive gains [8]. The usefulness of yoga therapy in managing antipsychotic-induced side effects in patients with schizophrenia has also been studied [9]. Some studies indicate that yoga and meditation may increase cortical thickness, particularly in the prefrontal cortex, and boost gray matter volume in brain areas critical for memory and cognition [10]. Hence, robust data is lacking in this section where very few studies reported about negative and cognitive symptom assessment after yoga therapy, so our study is to find out the effect of yoga on negative and cognitive symptoms through a randomized controlled trial.

METHODS

Study design and setting

A single-blind randomized controlled trial was conducted at a tertiary care hospital from June 2023 to June 2025. Sampling was done as per convenience sampling, but the allocation to Group A (interventional group) and Group B (non-interventional group) was randomized. Hence, external validity is limited. Computerized block randomization was used. As the assessor or rater was blinded, but the patients could not be blinded, it was a single-blind randomized controlled trial. (CONSORT 2025 Flow Diagram; Figure 1) [11].

Inclusion criteria

Patients (aged 18–60 years) were screened with the PANSS scale, and scores <75. Both male and female who gave informed consent were included for the study.

Exclusion criteria

Those who were suffering from other major psychiatric illnesses, severe physical illness, dementia, or mental retardation were excluded.

Sample size calculation

The sample size was calculated as 104 using G*Power software. Considering a 10% dropout rate, a total of 120 patients with schizophrenia were included in the study.

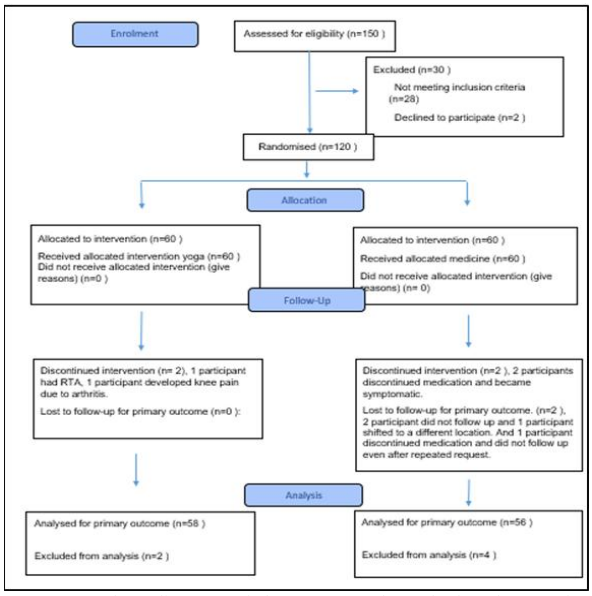

Figure 1: Flow diagram of the progress through the phases of a randomized trial of two groups (enrolment, intervention allocation, follow-up, and data analysis).

Intervention and outcome measurements

Procedure- All the patients with schizophrenia after diagnosis using ICD-10 were selected as per convenient sampling. Then patients were randomly allocated to two groups by computerized block randomization technique. Two groups were formed, comprised of 60 participants in each group: Group A, with patients who were given yoga intervention along with standard pharmacotherapy, and Group B, with patients who continued with the standard pharmacotherapy, i.e., olanzapine up to 30 mg. Doses were optimized as per the requirement of patients' symptoms, and the maximum dose was 30 mg. Once patients were recruited for the study, there was no change of dose for 3 months. Patients were on a single antipsychotic drug that is olanzapine, and a few of the patients were on Trihexyphenidyl 2.0 mg. Baseline PGIBBD score and SANS score were obtained from each participant. Yoga was given for 3 months to each participant, and the schedule for yoga sessions was Tuesday/Thursday/Saturday morning 8 am - 9 am, considering feasibility for patients to attend and continue in yoga therapy. After 3 months of follow-up, all the participants were assessed by the PGI BBD scale to see the changes in the assessment of cognitive symptoms and by the SANS (Scale for the Assessment of Negative Symptoms) scale to see the change in negative symptoms. Then group B patients who were on standard pharmacotherapy for 3 months were given yoga for the next 3 months, and it was given to group B as per the ethics committee's recommendation. But no crossover analysis was done.

Measurement tools

Tool 1, the **Scale for the Assessment of Negative Symptoms (SANS)** [12], is a clinician-rated instrument used to evaluate negative symptoms in individuals with schizophrenia and related psychotic disorders. It assesses five domains: affective flattening or blunting, alogia, avolition–apathy, anhedonia–asociality, and attentional impairment. Each item is rated on a severity scale based on behavioral observations and clinical interviews, with higher scores indicating greater symptom severity. Tool 2, the **PGI Battery of Brain Dysfunction (PGIBBD)** [13], is a standardized neuropsychological test battery developed by the Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, for the assessment of cognitive deficits associated with brain dysfunction. It evaluates multiple cognitive domains, including memory, attention, perceptuomotor skills, and executive functions, using a set of culturally appropriate tests for the Indian population. The PGIBBD is commonly used in clinical and research settings to assess the presence, pattern, and severity of cognitive impairment in neurological and psychiatric disorders. Tool 3, the **Color Trails Test (CTT)** [14], is a neuropsychological assessment tool used to evaluate attention, visual scanning, psychomotor speed, and executive functioning, particularly cognitive flexibility and set shifting. It consists of two parts: CTT–1, which primarily assesses sustained attention and sequencing, and CTT–2, which additionally measures divided attention and cognitive flexibility by requiring alternating color sequences. CTT is designed to be culturally fair, minimizing language dependence, and is widely used in clinical and research settings to assess cognitive functioning across diverse populations.

Yoga intervention

Yoga classes were led by an instructor from the university who has done a PhD in yoga. Yoga intervention was given for one hour on alternate days (Tuesday/Thursday/Saturday) inside the hospital in our department demonstration room from 8 am to 9 am. The yoga intervention was comprised of OM chanting for 10 min, Sasankasana for 10 min, Anulomvilom for 10 min, Ustrasana for 5 min, Tadasana for 15 min, sharing about patients' experiences for 5 min, and relaxation for 5 min.

Ethical considerations

The study protocol was approved by the institutional ethics committee. Written informed consent was taken from all the participants.

Statistical analysis

Statistical analysis was conducted using SPSS version 27, including both an independent *t*-test and a paired *t*-test. The independent *t*-test was applied to compare the mean values between two separate groups to determine whether there was a statistically significant difference between them. In contrast, the paired *t*-test was used to compare measurements taken from the same subjects at two different time points, allowing assessment of changes within the groups. All statistical significance was determined by *a p-value* less than 0.05. The primary outcome would be improvement in negative and cognitive symptoms of schizophrenia after yoga intervention as an add-on therapy.

RESULTS

Chi-squared test, unpaired t-test, and paired t-test were used for data analysis. The demographic and clinical characteristics of the participants at baseline are shown in Table 1.

Table 1: Sociodemographic profile of all the participants

Variables	Group A (n=58)	Group B (n=56)	Total (%)	*p*-value (chi-square)
Gender				
Male	27	31	50.9	0.347
Female	31	25	49.1	
Religion				
Hindu	56	56	98.2	0.161
Muslim	2	0	1.8	
Education				
Illiterate	2	0	1.8	
Primary	4	2	5.3	
Secondary	9	7	14	0.209
Higher secondary	25	19	38.6	
Graduate and above	18	28	40.4	
Occupation				
Unemployed	33	22	48.2	0.059
Employed	25	34	51.8	
Family income group				
Low income	19	16	30.7	0.561
Middle income	31	35	57.9	
Residence				
Habitat	8	5	11.4	
Urban	21	25	40.4	0.491
Rural	23	22	39.5	
Suburban	14	9	20.1	
Family type				
Nuclear	12	10	19.3	
Single	22	12	29.8	0.090
Joint	24	34	50.9	
Duration of illness (year)				
< 1.0	10	13	20.2	
1-5	15	14	25.4	0.723
1-6	33	29	54.4	

The present study compared the sociodemographic characteristics of participants in group A and group B to assess baseline comparability between the two groups. Overall, the two groups were largely comparable across most sociodemographic variables, indicating adequate matching. Gender distribution was almost equal in the total sample, with males and females represented in nearly similar proportions, and no statistically significant difference was observed between the two groups. Likewise, religion did not differ significantly, with the vast majority of participants belonging to the Hindu religion, reflecting the regional population profile. Educational status was broadly similar across both groups, with most participants having attained higher secondary education or above. Although group B had a slightly higher proportion of graduates and above compared to group A, this difference did not reach statistical significance. Occupational status, when it was compared between unemployed and employed groups,

showed no statistically significant difference found between the two groups.Group A had a higher proportion of unemployed participants, whereas group B had a greater proportion of individuals who were employed, suggesting differences in employment patterns between the groups. Family income distribution was comparable, with the majority of participants in both groups belonging to the middle-income category, followed by the low-income group. Habitat-wise distribution was also similar, with participants almost evenly distributed across urban and rural settings and a smaller proportion residing in suburban areas. Regarding family type, joint families were the most common in both groups, followed by single and nuclear families, and no significant intergroup difference was noted. Duration of illness was also comparable between the groups, with more than half of the participants in both groups reporting an illness duration of more than five years. There were 114 participants in two groups, and the groups were comparable at baseline in terms of gender, socioeconomic status, and duration of illness. The mean age of the participants in Group A and Group B (Table 2). The mean age of participants in Group A was 36.29±12.16 years, while the mean age in Group B was slightly higher at 39.07±11.03 years. The difference in mean age between the two groups was not statistically significant (p= 0.205), indicating that both groups were comparable with respect to age and that age was unlikely to have influenced the study outcomes. In Table 3 negative symptom scores and PGIBBD domain scores were compared between the groups and within the group after yoga intervention.

Table 2: Age distribution of participants

Age groups (year)	Mean Age	*p*-value
A	36.29±12.16	0.205
B	39.07±11.03	

The mean SANS score before intervention in Group A was 33.0±7.7. After intervention in Group A, it was reduced to 14.52±7.04. While in group B, at baseline the mean SANS score was 33.63±4.98, and after 3 months the mean SANS score was 29.93±4.35. Similarly, in each domain of PGIBBD, the mean score in each domain reduced significantly in group A compared to group B. In attention and concentration domains after 3 months of intervention, group A improved substantially (12.55 ± 1.55) compared to group B (9.84 ± 0.89). But when they were compared, there was no statistically significant difference found. At 3 months, group A improved more (8.78 ± 0.99) than group B (6.48 ± 1.09) in delayed recall. When the delayed recall domain was compared between group A and group B, it was non-significant. At 3 months, group A (9.22 ± 0.87) improved more than group B (7.16 ± 0.75) in immediate recall. After 3 months, group A (8.67 ± 0.84) outperformed group B (6.09 ± 0.99) in verbal retention for similar pairs. Immediate recall and verbal retention for similar pairs when compared between group A and group B, a significant difference was observed. When verbal retention for dissimilar pairs was compared between group A and group B, there was no statistically significant difference found. But group A showed greater improvement after 3 months (10.03±1.02 *vs*. 8.52±0.73) in verbal retention for dissimilar pairs. All the domains of PGIBBD were compared within the groups; there was a statistically significant difference between the groups. The CTT 1 and CTT 2 tests have 3 and 4 domains, respectively. The mean score of each domain was compared between the groups. After 3 months, both groups demonstrated a marked and statistically significant reduction in scores across all CTT domains for CTT-1 (Q1–Q3) and CTT-2 (Q1–Q4); the paired t-test showed highly significant improvements in both Group A and Group B (p< 0.001). Mean scores decreased substantially from baseline to 3 months in each domain, reflecting significant improvement in both group A and group B. To avoid type 1 error for multiple domain comparisons, we applied false discovery rate (Benjamin-Hochberg) corrections separately to within-group and between-group analyses.

Table 3: Distribution of negative symptoms score and PGIBBD domain scores

Variables	Group A	Group B	Paired t-test for group A	Paired t-test for group B	*p*-value* at 3 Mo
Baseline SANS score	33.00±7.70	33.63±4.98	<0.001	<0.001	<0.001
SANS after 3 Months	14.52±7.04	29.93±4.35			
Baseline attention concentration	9.57±1.04	9.30±1.14	<0.001	<0.001	0.198
Attention concentration after 3 Months	12.55±1.55	9.84±0.89			
Baseline Delayed recall	5.02±0.94	5.16±0.826	<0.001	<0.001	0.391
Delayed recall after 3 Months	8.78±0.99	6.48±1.09			
Baseline Immediate recall	6.59±0.879	6.11±0.65	<0.001	<0.001	0.001
Immediate recall after 3 Months	9.22±0.87	7.16±0.75			
Baseline verbal retention for similar pairs	5.47±0.68	5.11±0.65	<0.001	<0.001	0.005
Verbal retention for similar pairs after 3 Months	8.67±0.84	6.09±0.99			
Baseline verbal retention for dissimilar pairs	8.21±1.02	8.05±1.10	<0.001	<0.001	0.443
Verbal retention for dissimilar pairs after 3 Months	10.03±1.02	8.52±0.73			

Values are expressed as mean±SD. SANS: Scale for Assessment of Negative Symptoms.* unpaired t-test.

The adjusted p value was mentioned in Table 4. The overall pattern of results remained unchanged; between group analysis remained statistically significant, while between-group differences remained nonsignificant. Table 5 describes the mean score changes with yoga intervention (Group A) and without yoga intervention (group B). The difference in mean score was found to be significantly improved in the intervention group compared to the nonintervention group. Group A demonstrated a markedly greater reduction in the total SANS score (24.98 ± 9.42) compared to group B (6.82 ± 4.17). The difference between the groups was highly

statistically significant ($p< 0.001$), indicating superior improvement in negative symptoms in group A. Significantly greater improvements were observed in group A across all assessed cognitive domains, such as attention and concentration.

Table 4: CTT(Color Trails Test) distribution in various domains

CTT Domains	Group A	Group B	Paired t-test (group A)	Paired t-test (group B)	Unpaired t-test (group A *vs*. group B at 3 Mo)	FDR adjusted *p*-value
Baseline CTT1 Q1 CTT Q1 after 3 Months	3.19±0.54 0.45±0.53	3.29±0.45 0.34±0.53	<0.001	<0.001	0.31	0.539
Baseline CTT1Q2 CTT1 Q2 after 3 Months	3.09±0.53 0.33±0.47	3.23±0.53 0.3±0.46	<0.001	<0.001	0.151	0.539
Baseline CTT1 Q3 CTT1 Q3 after 3 Months	5.17±0.566 1.02±0.35	5.25±0.51 0.63 ±0.55	<0.001	<0.001	0.446	0.539
Baseline CTT2 Q1 CTT2 Q1 after 3 Months	3.48±0.53 0.81±0.63	3.46±0.53 0.7±0.63	<0.001	<0.001	0.855	0.855
Baseline CTT2 Q2 CTT 2 Q2 after 3 Months	3.55±0.5 0.64±0.55	3.48±0.5 0.5±0.5	<0.001	<0.001	0.462	0.539
Baseline CTT2 Q3 CTT2 Q3 after 3 Months	3.71±0.49 0.6±0.56	3.61±0.56 0.39±0.49	<0.001	<0.001	0.317	0.539
Baseline CTT2 Q4 CTT2 Q4 after 3 Months	6.21±0.64 1.33±0.65	5.95±0.69 1.18±0.57	<0.001	<0.001	0.40	0.539

Values are presented as mean±SD. CTT1 Q1: Color Trails Test1 Error, CTT1 Q2: Color Trails Test2 Near-Missing, CTT1 Q3: Color Trails Test3Prompts. CTT2 Q1: Color Trails Test1 Color Error, CTT2 Q2: Color Trails Test2 Number Error, CTT2 Q3: Color Trails Test3 Near Missing, CTT2 Q4: Color Trails Test4 Prompts, FDR: False Discovery rate.

Table 5: Change of mean difference between group A and group B

Variables	SANS (group A)	SANS (group B)	*p*-value*
SANS	24.98±9.42	6.82±4.17	<0.001
Attention and concentration	2.98±0.86	0.54±0.83	<0.001
Delayed recall	3.76±0.61	1.32±0.76	<0.001
Immediate recall	2.64±0.91	1.05±0.81	<0.001
Verbal similarity	3.21±0.91	0.98±0.9	<0.001
Verbal dissimilarity	1.82±0.03	0.47±0.11	<0.001

Values are presented as mean±SD.* Unpaired *t*-test.

Group A showed a significantly higher mean improvement (2.98 ± 0.86) compared to group B (0.54 ± 0.83) ($p< 0.001$). Improvement in the delayed recall domain was greater in group A (3.76 ± 0.61) than in Group B (1.32 ± 0.76), with a statistically significant difference ($p< 0.001$). In immediate recall, group A demonstrated significantly greater gains (2.64 ± 0.91) compared to group B (1.05 ± 0.81) ($p< 0.001$). Similarly in the verbal similarity domain, the mean difference in group A (3.21 ± 0.91) was significantly higher than that in group B (0.98 ± 0.90) ($p< 0.001$). The verbal dissimilarity domain also showed significantly greater improvement in group A (1.82 ± 0.03) compared to group B (0.47 ± 0.11) ($p< 0.001$).

DISCUSSION

Overall, there were no statistically significant differences observed between group A and group B across the sociodemographic variables studied, suggesting that the two groups were comparable and that these factors were unlikely to have confounded the study outcomes. The difference in mean age between the two groups was not statistically significant ($p= 0.205$), indicating that both groups were comparable with respect to age and that age was unlikely to have influenced the study outcomes. The findings presented in the table demonstrate significant changes across clinical and cognitive variables in both groups over the three-month study period. At baseline, group A and group B exhibited comparable levels of psychopathology and cognitive performance, as reflected by SANS scores, attention, memory, and verbal retention scores. This baseline comparability suggests that any subsequent differences are likely attributable to the intervention rather than pre-existing group disparities. A pilot study was conducted in 2011 with an RCT randomizing 18 inpatients with schizophrenia to 8 weeks of yoga therapy or a waitlist and showed improvement in both positive and negative symptoms [16]. Following three months of intervention, Group A showed a marked and statistically significant reduction in symptom severity, with substantial improvements observed in both negative and cognitive symptom domains as measured by SANS scores and PGIBBD scores. In contrast, group B demonstrated only modest improvements, with symptom scores remaining relatively elevated at follow-up. The paired t-test results indicate that these changes within Group A were highly significant, highlighting a robust therapeutic effect. A review of the role of yoga in schizophrenia reported that quality of life, cognitive symptoms, and negative symptoms improved with add-on yoga therapy in schizophrenia, with a pooled mean effect size of 0.8, 0.6, and 0.4, respectively [17]. In a recent study, it was found that there are potential benefits of yoga as an adjunctive treatment in schizophrenia, particularly in addressing negative symptoms and improving aspects of quality of life [18], but they did not study the cognitive symptoms. In addition to clinical improvement, group A exhibited pronounced gains in cognitive functioning. Significant enhancements were observed in attention and concentration, immediate recall, delayed recall,

and verbal retention for both similar and dissimilar word pairs. These improvements suggest a broad-based enhancement in cognitive processing and memory consolidation over the study period. While group B showed slight improvements in some cognitive domains, the magnitude of change was comparatively smaller and less clinically meaningful. One meta-analysis concluded the effects of physical exercise on cognitive performance in people with schizophrenia included 10 controlled trials and a total of 385 participants. They found a significantly small-to-moderate positive effect on global cognitive performance, with no significant statistical heterogeneity [19]. As per ethical recommendations, group B patients who were followed for only 3 months with medications were given yoga therapy for the next 3 months, i.e., the patients were followed for a total of 6 months. In the results of 3 months' intervention, there was significant improvement in negative and cognitive symptoms in group A; adding yoga to the second group will be obviously statistically significant from the baseline measure, but no analysis was done for this observation. When the mean difference of various domains of the PGI BBD scale was compared between the groups, a statistically significant difference was found (Table 5). It was found that the improvement in group A participants was significantly greater than group B's in every domain of negative and cognitive function assessment. Another randomized controlled trial reported yoga intervention improved the immune inflammatory pathway, leading to an overall improvement in psychotic symptoms [20].

Study limitations

To overcome logistic obstacles, we made video calls to some of the patients who did not turn up for Yoga at our hospital; this could be uneven intervention at the hospital and at home. We taught them yoga and scrutinized yoga through video calls on particular days so that there will be no dropout and missing of intervention. We could provide intervention for 3 months and 3 days a week. In the future, if Yoga can be given daily for a longer duration, a better effect might come.

Conclusion

The pattern of results suggests that the intervention administered to group A was more effective in reducing psychopathological symptoms and enhancing cognitive performance than the non-intervention group, B. The concurrent improvement in both symptom severity and cognitive measures in Group A underscores the potential role of this intervention in addressing not only clinical symptoms but also associated cognitive deficits, which are critical determinants of functional outcome.

Conflict of interests

The authors declared no conflict of interest.

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The authors did not receive any source of funds.

Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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