Curr Behav Neurosci Rep (2017) 4:209–220
DOI 10.1007/s40473-017-0125-6

PSYCHOSIS (A AHMED, SECTION EDITOR)

# Yoga for Schizophrenia: a Review of Efficacy and Neurobiology

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Published online: 28 July 2017
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**Abstract**
*Purpose of Review* Schizophrenia is a debilitating psychiatric illness requiring multimodal treatments. Besides pharmacotherapy, several adjunct treatments have been recommended, including yoga. We review recent findings speaking to yoga's efficacy and towards gaining a better understanding of why yoga may affect positive change, evidence on putative neurobiological mechanisms.
*Recent Findings* Recent research with schizophrenia patients suggests that yoga may lead to improvements in symptoms, cognition, and functioning. These changes may occur through a variety of mechanisms including yoga-induced changes in neural plasticity, the neural mechanisms supporting internal mentation, oxytocin release, BDNF, and other factors. We review reports of possible mechanisms through which yoga is believed to impact response in schizophrenia.
*Summary* Our current review cannot provide a conclusive statement on the use of yoga as a standard treatment for schizophrenia; however, the available evidence suggests that yoga may positively impact aspects of the illness in patients with schizophrenia. Further research with adequately powered randomized controlled trials is essential.

**Keywords** Yoga therapy · Yogasana · Meditation · Neurobiology · Schizophrenia · Psychosis

This article is part of the Topical Collection on *Psychosis*

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## Introduction

Schizophrenia is a chronic, debilitating psychiatric disorder, characterized by distortions in reality, thinking, cognition, and affect. Antipsychotic medications have remained the mainstay of treatment since the 1950s [1]. Though effective at targeting positive symptoms (i.e. hallucinations, delusions), these agents are far from a panacea. Aside from pernicious side effects, their efficacy at targeting other aspects of the illness, including negative symptoms (e.g. diminished emotional experience and expression), cognitive deficits, and social impairment, is limited [2–4]. Furthermore, owed in part to intolerability and limited efficacy for all symptoms associated with the disorder, discontinuation rates for patients on antipsychotic drugs are quite high [5].

Of course, for a disorder whose sequela is so all-encompassing and complex, it would be naïve to believe that single treatment—pharmaceutical, psychosocial, or otherwise—will relieve all sources of suffering for those with the illness. This makes it incumbent upon clinicians and researchers to explore the efficacy of multimodal treatment approaches that help to target the totality of disorder. Adjunctive treatments that comprise a multimodal approach should be more than just efficacious; they should be tolerable, durable,

and feasible to implement in the community. Do such treatments exist for people with schizophrenia? In addition to cognitive training and aerobic exercise, recent work has suggested that yoga may also fit the bill [6, 7•]. Preliminary evidence suggests that yoga may ameliorate symptoms, cognitive deficits, and impaired functioning for people with schizophrenia, and may do so by inducing enduring neurobiological change. Here, we review these findings speaking to the efficacy of yoga as an adjunctive treatment for schizophrenia, possible mechanisms of action, and outline future directions for the field.

## The Practice of Yoga and Its Health Benefits

Yoga is a spiritual, meditative, and physical practice involving mental and physical components designed to help practitioners achieve the unification and optimal functioning of mind and body [8–10]. Yoga practice typically involves a series of physical postures (*āsanas*), breathing techniques (*prānāyāma*), and meditative/mindfulness practices (*dyana*) [9]. There exists many different forms of yoga, each of which prioritize different components [11]. For example, Hatha yoga, which emphasizes physical postures, breath, and meditation, is commonly practiced in Western cultures and includes popular subtypes such as Bikram, Iyengar, and Ashtanga [12, 13].

Yoga is widely practiced, representing one of the most widely used complementary health approaches in the USA, and the most widely used mind and body practice [14]. Approximately 31 million adults in the USA have ever practiced yoga, with 21 million practicing in a 12-month period [14]. Furthermore, its practice is on the rise with estimates of 12-month prevalence from the 2012 NHIS survey at 9.5% compared to 6.1% in 2007 and 5.1% in 2002 [15].

The majority of practitioners (78.4%) report practicing yoga for well-being and disease prevention [14], and for good reason. Research has demonstrated positive effects of yoga on a wide variety of medical conditions including pain [16, 17], cardiovascular disease, hypertension, and associated risk factors [18, 19], and metabolic conditions [19–21], among many other medical issues [17]. Yoga's benefits appear to extend beyond the realm of physical health to mental health as well. Research has shown positive effects of yoga on stress, anxiety, depression, and associated physiological measures [22]. Preliminary evidence also suggests that yoga may be beneficial to people with a variety of psychiatric disorders, including mood disorders [23], anxiety disorders [24], OCD [25], PTSD [26], ADHD [27], and eating disorders [28]. Though the precise mechanisms mediating positive changes as a result of yoga practice are unknown, research suggests that yoga positively impacts the neurobiological mechanisms related to stress and mood reactivity [22], possibly through its effect on cortisol release [29], and may confer neuroprotective effects [30–32].

## The Effect of Yoga on Schizophrenia

Does practicing yoga lead to similar benefits in people with schizophrenia? Several studies have examined this question, using an array of yoga protocols, comparison groups (e.g. waitlist controls, treatment-as-usual, aerobic exercise), and outcome measures (e.g. assessments of positive symptoms, negative symptoms, general psychopathology, cognition, social/occupational functioning, and quality of life). These studies are summarized in Table 1.

On symptoms, many studies have found evidence that compared to active (e.g. exercise) and non-active control conditions, yoga confers improvements to positive symptoms, negative symptoms, and general psychopathology (e.g. anxiety, depression), which are estimated to be small- to medium-sized effects [46••]. Compared to positive symptoms, it appears that though yoga may more consistently impact negative symptoms and to a larger magnitude [46••], the durability of these changes is unclear as few studies include follow-ups and those that do demonstrate mixed evidence.

Relative to symptoms, fewer studies have examined yoga's effect on cognition. Three studies that have examined yoga's effect on non-social cognition demonstrated improvements in attention (although one only found improvement at 6-month follow-up, [33•]). Separately, these studies also found support for improvement to abstraction and different aspects of memory including spatial memory, verbal memory, and working memory [34, 40]. One study that examined the durability of these findings found improvements in abstraction/mental flexibility, attention, and spatial memory 3- to 6-months post-intervention. A recent meta-analysis found support for yoga improving verbal memory and improving attention/executive functioning at a trend level, both of which were small effects [46••]. A small number of studies have examined yoga's effect on social cognition [35, 39]. Two studies found improvement in emotion recognition post-intervention, which in one study, was not maintained at follow-up. Another study found improvements in face memory, which were present at 6-month follow-up and emotion processing only at 6-month follow-up. Yoga's effects on social cognition are of particular interest given the strong relation between social cognitive deficits in schizophrenia and real-world social functioning [47]. It is interesting that yoga would lead to any improvement in social cognition at all. One possibility is that there exists some non-specific positive social effect of yoga from performing the practice in a group format with other participants and interacting with an instructor. Another possibility is that compared to other active group interventions, there exists some specific component of yoga practice, for example, promoting social connection (see section below), that confer the benefit to social ability [48]. Future work can tease these possibilities apart by making sure to include control interventions that also have a social component.

**Table 1** Studies evaluating the effects of yoga for schizophrenia

| Study | Sample characteristics | Intervention | | Outcomes assessed (measure) [timepoints][a] | Main findings | | Notes |
|---|---|---|---|---|---|---|---|
| | | Yoga | Control | | Short-term | Long-term | |
| Bhatia et al. [33•] | 286 outpatients with schizophrenia, ≥ 18-years-old, clinically stable, no substance abuse in past 6 months, no neurological/medical disorder, prior yoga practice | *Yoga plus Treatment-As-Usual:* Postures, breathing, "weekly nasal cleansing"; 21 consecutive days except Sundays and holidays, 1 h sessions of supervised training by instructor, followed by at-home practice (tracked with compliance records) ($n$ = 104) | *(1) Physical Exercise Training.* Same as Duraiswamy et al. (2007). *(2) Treatment-As Usual.* | Abstraction and mental flexibility, attention, working memory, verbal memory, face memory, spatial memory, spatial processing, language, sensorimotor dexterity, emotion processing (Penn Computerized Neuropsychological Battery) [post-intervention, 3 month follow-up, 6 month follow-up] | *Yoga > TAU:* Spatial memory speed, face memory speed. *Physical Exercise > TAU:* Face memory accuracy/speed, working memory accuracy/speed. *Physical Exercise > Yoga:* Face memory accuracy. | 3 months, Yoga > TAU*:* Abstraction and mental flexibility accuracy. *3 months, Physical Exercise > TAU:* Face memory accuracy. *3 months, Physical Exercise > Yoga:* Face memory accuracy. *6 months, Yoga > TAU:* Emotion memory speed, face memory speed, spatial memory speed. *6 months,* Physical Exercise > TAU**:** Attention accuracy, face memory accuracy, emotion speed. *6 months, Yoga > Physical Exercise:* attention accuracy. *6 months, Physical Exercise > Yoga:* Working memory accuracy. | |
| Bhatia et al. [34] | 65 outpatients with schizophrenia, ≥ 18-years-old, no alcohol or substance dependence or neurological disorder | Asanas, pranayama, om chanting (protocol provided at http://www.indouspgp.info/publications/400); 1 h/day, 21 consecutive days except Sunday with qualified yoga instructor ($n$ = 30) | *Medication Management*: "Conventional pharmacological and non-pharmacological treatment" ($n$ = 23) | Abstraction and mental flexibility, attention, working memory, verbal memory, face memory, spatial memory, spatial processing, language, sensorimotor dexterity, emotion processing (Penn Computerized Neuropsychological Battery) [post-intervention, 2 month follow-up] | *Yoga > Control*: abstraction speed, attention speed | *Yoga > Control*: attention accuracy, abstraction speed, attention speed | Not randomized, concurrent treatment not controlled |
| Behere et al. [35] | 91 outpatients with schizophrenia, 18–60 years old, stabilized on antipsychotics, no | SVYASA yoga module consisting of "loosening exercises, breathing practices, suryanamaskara, sitting, | *(1) Exercise*: Adapted from National Fitness Corps – Handbook for Middle High and Higher Secondary Schools, | Positive Symptoms (PANSS), Negative Symptoms (PANSS), Social- Occupational Functioning (SOFS), | *Yoga<>Controls*: Not tested. *Improvements Within Yoga Group:* positive symptoms, negative symptoms, | *Yoga<>Controls*: Not tested. *Improvements Within Yoga Group:* Positive symptoms, negative symptoms. | Adherence to yoga/exercise intervention unknown, authors do not |

**Table 1** (continued)

| Study | Sample characteristics | Intervention | | Outcomes assessed (measure) [timepoints][a] | Main findings | | Notes |
|---|---|---|---|---|---|---|---|
| | | Yoga | Control | | Short-term | Long-term | |
| | psychiatric/medical comorbidities, CGI ≤ 3 | supine, and prone posture asanas along with pranayama and relaxation techniques"; 1 month training by yoga instructor followed by 2 months in-home practice, 1 h/session ($n$ = 34) | consisting of "brisk walking, jogging, and exercises in standing and sitting postures and relaxation" ($n$ = 31); 1 month training by instructor followed by 2 months in-home practice, 1 h/session. *(2) Waitlist* ($n$ = 26). | Emotion Recognition (TRENDS) [post-intervention, 4 month follow-up] | emotion recognition, social-occupational functioning. *Improvements Within Waitlist:* Social-occupational functioning. | | assess Group*Time interaction |
| Duraiswamy et al. [36] | 61 inpatients and outpatients with schizophrenia, 18–55 years old, stabilized on antipsychotics, no comorbid severe physical illness, mental retardation or substance dependence, CGI ≥ 4 | Same yoga protocol as Behere et al. [35]; 15 days of training by instructor, 1 h/day, 5 days/week, 3 weeks, followed by 3 months practice at same frequency ($n$ = 31) | *Physical Training:* Same exercise protocol as Behere et al. [35]; 15 days of training by instructor, 1 h/day, 5 days/week, 3 weeks, followed by 3 months practice at same frequency ($n$ = 30) | Positive Symptoms (PANSS), Negative Symptoms (PANSS), Depression (PANSS), Angeria (PANSS), Total Symptoms (PANSS), Social-Occupational Functioning (SOFS), Quality of Life (WHOQOL-BREF) [post-intervention] | *Yoga > Control:* negative symptoms, depression, anergia, total symptoms, social-occupational functioning, quality of life | Not assessed | |
| Ikai et al. [37] | 49 outpatients with schizophrenia or related disorder, ≥ 18-years-old, stabilized on antipsychotics, no current substance/alcohol abuse/dependence | "Gentle yoga stretches and simple movements in coordination with breathing as follows: warm-ups and loosening-up exercises (gentle movements of major muscle groups, joint rotations and self-massage), asana (twisting poses, standing poses and sun salutation), deep relaxation (corpse pose) and breathing exercises"; 8 yoga session with trained instructor, 1 h/week for 8 weeks ($n$ = 25) | *Regular Day-Care*: "Weekly regular day-care program (e.g., social skills training, psychoeducation) for 8 weeks" ($n$ = 24) | Total Symptoms (PANSS), Positive Symptoms (PANSS), Negative Symptoms (PANSS), General Psychopathology (PANSS), Psychosocial functioning (FACT-Sz), Quality of Life (EQ-5D) [post-intervention, 16 week follow-up] | *Yoga > Control:* Negative symptoms, psychosocial functioning | *Improvements Within Yoga Group:* Quality of life | Follow-up not performed with control group |
| Ikai et al. [38] | 50 outpatients with schizophrenia or related disorder, ≥ 18-years-old, stabilized on medication, | Same intervention as Ikai et al. [37]. Hatha yoga consisting of "gentle yoga stretches and simple | *Treatment-as-usual*: Same intervention as Ikai et al. [37]. "Weekly regular daycare program (which | Same as Ikai et al. [37] and BDNF [post-intervention, 16 week follow-up] | No difference | No difference | Follow-up not performed with control group |

**Table 1** (continued)

| Study | Sample characteristics | Intervention | | Outcomes assessed (measure) [timepoints][a] | Main findings | | Notes |
|---|---|---|---|---|---|---|---|
| | | Yoga | Control | | Short-term | Long-term | |
| | no current alcohol abuse or psychiatric comorbidities | movements in coordination with breathing (gentle movements of major muscle groups), asana (twisting poses and standing poses), deep relaxation, and breathing exercises"; 8 weekly 1 h sessions ($n$ = 25) | provided social skills and walking)" for 8 weeks ($n$ = 25) | | | | |
| Jayaram et al. [39•] | 43 inpatients and outpatients with schizophrenia, ages 18–45 years, stabilized on antipsychotics, CGI ≤ 3, no psychoactive substance dependence in past 6 months or abuse in past 1 month, no comorbid neurological or medical illness | "Loosening exercises, breathing practices, Suryanamaskāra, sitting and supine and prone posture āsanas along with Prāṇāyāma and relaxation techniques"; 1 h/session, for 1 month with professional yoga therapist ($n$ = 15) | *Waitlist,* $n$ = 26 | Positive Symptoms (SAPS), Negative Symptoms (SANS), Social-Occupational Functioning (SOFS), Emotion Recognition (TRENDS), Plasma Oxytocin [post-intervention] | *Improvements Within Yoga Group*: positive symptoms, negative symptoms, social-occupational functioning, emotion recognition, plasma oxytocin. *Improvements Within Control Group:* positive symptoms, negative symptoms. | Not assessed | Authors do not assess Group*Time interaction |
| Lin et al. [40] | 124 female outpatients with schizophrenia spectrum disorder diagnosed within 5 years of recruitment, ages 16–60 years | Classic Hatha Yoga consisting of breathing control, body postures, relaxation; 60 min/session, 3 sessions/week, 12 weeks, led by qualified yoga instructor ($n$ = 45) | *(1) Aerobic Exercise*: Walking on a treadmill, stationary cycling, cool-down stretching; 60 min, 3 sessions/week, 12 weeks ($n$ = 40); *Waitlist* ($n$ = 39) | Verbal Memory (Hong Kong List Learning Test), Working Memory (Digit Span), Attention (Letter Cancelation Test), Executive Function (Stroop), Positive Symptoms (PANSS), Negative Symptoms (PANSS), General Psychopathology (PANSS), Depression (Calgary Depression Scale), Structural MRI, Quality of Life (SF-36) [post-intervention, 18 month follow-up] | *Yoga > Waitlist Exercise:* Verbal memory, working memory, attention, negative symptoms, general psychopathology, depression, quality of life | *Yoga > Waitlist:* Verbal memory, working memory, attention, negative symptoms, general psychopathology, depression | Yoga not compared to aerobic exercise |
| Lin et al. [41•] | Same as Lin et al. [40] | Same as Lin et al. [40] ($n$ = 23) | Same as Lin et al. [40], *(1) Aerobic Exercise* ($n$ = 23). *(2) Waitlist* ($n$ = 12) | fMRI, amplitude of low-frequency fluctuations (ALFF) | *Yoga > Aerobic Exercise, Waitlist:* decreased ALFF in precuenus; ALFF changes in precuenus | Not assessed | |

**Table 1** (continued)

| Study | Sample characteristics | Intervention | | Outcomes assessed (measure) [timepoints][a] | Main findings | | Notes |
|---|---|---|---|---|---|---|---|
| | | Yoga | Control | | Short-term | Long-term | |
| | | | | | correlated with changes in negative symptoms | | |
| Manjunath et al. [42] | 88 inpatients with non-affective psychotic disorder | Yoga plus standard pharmacotherapy (procedure adopted from Duraiswamy et al., 2007); daily 1 h sessions for 2 weeks followed by 4 weeks of practice for total of 1.5 months | *Physical Exercise Plus Standard Pharmacotherapy* (procedure adopted from Duraiswamy et al., 2007); daily 1 h sessions for 2 weeks followed by 4 weeks of practice for total of 1.5 months | Positive Symptoms (PANSS), Negative Symptoms (PANSS), General Psychopathology (PANSS), Clinical Severity (CGI), Depression (HDRS) [2 weeks after baseline, post-intervention] | *Yoga > Control (post-intervention):* illness severity, depression | | Significant drop-out rate with completers different from non-completers on several variables, treatment adherence after 2-weeks unclear |
| Paikkatt et al. [43] | 18 male inpatients with schizophrenia, ages 20–50 years, 2 year minimum illness duration, mild-moderate symptoms, no history of substance dependence, mental retardation, organic mental disorder, head injury, or neurological disorder | Yoga plus pharmacotherapy*:* Postures/asanas and pranayama/breathing exercises; 1.5 h/session, everyday for 1 month conducted by trained yoga teacher ($n$ = 9) | *Pharmacotherapy alone* ($n$ = 9) | Positive Symptoms (PANSS), Negative Symptoms (PANSS), General Psychopathology (PANSS) [post-intervention] | *Yoga > Control (post-treatment):* delusion, conceptual disorganization, blunted affect, emotional-, passive and active social withdrawal, difficulty in abstract thinking, somatic concern, guilt feelings, depression, motor retardation, unusual thought content, disorientation, preoccupation, | Not assessed | Authors do not evaluate Group*Time interaction |
| Vancampfort et al. [44•] | 40 inpatients with schizophrenia or schizoaffective disorder, no psychiatric comorbidity, no significant cardiovascular, neuromuscular, or endocrine condition, CGI ≥ 4 | Hatha Yoga consisting of cardiovascular warming-up exercises, abdominal breathing exercises, asanas, relaxation techniques (shavasana); single 30 min session ($n$ = 40) | *(1) Aerobic Exercise*: "Cycling for 20 min at a self-selected intensity with heart rate feedback"; single 20 min session ($n$ = 40); *(2) No Exercise*: Read in a waiting room for 20 min ($n$ = 40) | State Anxiety (STAI), Psychological Stress (SEES), Subjective Well-Being (SEES) [post-intervention] | *Yoga > No Exercise:* state anxiety, psychological stress, subjective well-being. *Yoga<>Aerobic Exercise:* No differences. | Not assessed | |
| Varambally et al. [10] | 120 outpatients with schizophrenia, stabilized on antipsychotic medication, moderately symptomatic (CGI ≥ 3), no ECT in past 3 months | Same protocol as Duraiswamy et al. (2007): Yogasana consisting of "certain postures and breathing patterns"; 45 min | Same protocol as Duraiswamy et al. (2007) *(1) Exercise*: 45 min sessions, 25 sessions in first month ($n$ = 37). *(2) Waitlist:* | Positive Symptoms (PANSS), Negative Symptoms (PANSS), Total Symptoms (PANSS), Social-Occupational | *Yoga > Exercise, Waitlist (proportion of patients showing improvement):* negative symptoms, total symptoms, | Not assessed | |

**Table 1** (continued)

| Study | Sample characteristics | Intervention | | Outcomes assessed (measure) [timepoints][a] | Main findings | | Notes |
|---|---|---|---|---|---|---|---|
| | | Yoga | Control | | Short-term | Long-term | |
| | | sessions, 25 sessions in first month taught by certified yoga teacher, followed by 3 months of at-home practice ($n$ = 47) | Treatment-as-usual for 4 months ($n$ = 36) | Functional (SOFS) [post-intervention] | social-occupational functioning | | |
| Visceglia and Lewis [45] | 18 "clinically stable" inpatients with schizophrenia | Breath-centered yoga consisting of "pranayama (breathing exercises), warm-ups (gentle movements of major muscle groups and joint rotations), asana (yoga postures that always included at least one of each the following types of postures: forward bends, back bends, twists, inversions, standing, and balancing postures), and yoga nidra (deep relaxation)"; twice weekly, 45 min/session, 8 weeks with instructor ($n$ = 10) | *Waitlist* ($n$ = 8) | Positive Symptoms (PANSS), Negative Symptoms (PANSS), General Psychopathology (PANSS), Total Symptoms (PANSS), Quality of Life (WHOQOL-BREF) [post-intervention] | *Yoga* > *Waitlist:* positive symptoms, negative symptoms, general psychopathology, total symptoms, quality of life | Not assessed | |

*PANSS* Positive and Negative Symptom Scale, *SOFS* Social-Occupational Functioning Scale, *TRENDS* Tool for Recognition of Emotions in Neuropsychiatric Disorders, *WHOQOL-BREF* World Health Organization Quality of Life, *FACT-Sz* Functional Assessment for Comprehensive Treatment of Schizophrenia, *EQ-5D* EuroQol 5 Dimensions Classification Systems, *SF-36* The Short Form Health Survey, *CGI* Clinical Global Impression Scale, *HDRS* Hamilton Depression Rating Scale

[a] We report only on outcomes related to psychopathology, cognition, functioning, quality of life, and relevant neurobiological measures

On quality of life and social-occupational functioning, studies fairly consistently demonstrate that yoga confers benefits to these areas, which are small- to medium-sized effects [46••]. Few studies that measure quality of life or social-occupational functioning included a follow-up, although one that did found that improvements in quality of life persisted [37] while another found no improvement in quality of life or social-occupational functioning post-intervention or at follow-up [38].

These findings should be considered in the context of several important limitations affecting the quality of the evidence presented [49, 50]. Most notably, sample sizes are extremely small, ranging from 9 to 47 participants in the yoga group,[1] most trials are single-blind (although it may be difficult to double-blind an intervention of this nature), concurrent treatment is not always controlled, and adherence to the yoga or control protocol is unclear. There also exists substantial heterogeneity in the yoga protocol itself in terms of intervention components (e.g. emphasis on certain postures, breathing techniques, or meditation), duration, intensity of practice, and inclusion and quality of yoga instruction. Despite the view that yoga practice should be adapted to the specific needs and goals of the practitioner [45], standardizing and validating specific yoga protocols will go a long way in establishing the efficacy of yoga as an intervention [51]. These limitations notwithstanding the available evidence suggest that yoga may be beneficial in the short-term to people with schizophrenia, contributing to improvements in symptoms, cognition, functioning, and quality of life. There is some evidence to suggest that some of these improvements are durable, but additional work is needed before drawing a strong conclusion.

## Putative Neurobiological Mechanisms

The exact mechanisms of how yoga affects change in schizophrenia are unknown. However, there exist at least several studies that have included measures of neurobiology that may better speak to yoga's mechanism of action in schizophrenia. Researchers have also proposed many different routes through which yoga may affect the changes described above.

Schizophrenia has been conceptualized as an illness of neuronal disconnectedness. Yoga is said to have effects on several regions of the brain including prefrontal cortex, inferior parietal lobule, insula, and amygdala, regions that are implicated in the disconnectivity [52•]. Yoga may foster brain plasticity and neurogenesis in schizophrenic subjects thereby improving functional outcomes [41•]. One possibility is that by manipulating focused attention, yoga leads to changes in the neural mechanisms supporting internal mentation. In support of this idea, one neuroimaging study of schizophrenia patients, evaluating spontaneous low-frequency fluctuations in BOLD signal demonstrated a post-yoga decrease in the precuneus, compared to a waitlist control group [41•]. The precuneus has been implicated as a hub in the brain's default network—a network of brain regions that are preferentially engaged during stimulus-independent, internal mentation, such as self-referential processing or mind-wandering [53]. Other neuroimaging studies have found decreased precuneus activity in experienced meditators during meditation [54]. Taken with the patient data, yoga may alter mind-wandering tendencies and promote present-focused as opposed self-focused attention.

Physical exercise is believed to enhance memory and neuronal plasticity. In fact, aerobic exercise can lead to alteration in hippocampal volume or cortical thickness thus impacting overall cognition-working memory, processing speed, and visual learning [55]. A review article comparing exercise and yoga highlighted several advantages of yoga including emphasis on breathing and mindfulness, thereby indicating that yoga may be equal to or in some cases superior to exercise [56]. Animal experiments have demonstrated hippocampal neurogenesis with exercise. In a randomized controlled trial in schizophrenic patients, MRI findings revealed that exercise induced increase in hippocampal volume [57]. Antipsychotic medications are said to mediate their effects via neuronal transmission by altering gene expression and neuronal plasticity [58]. Although the exact mechanism of yogasana is not clear, it can be speculated that the exercise component in yoga has the potential of improving symptoms and functioning in schizophrenia by altering neuronal transmission.

Another possibility is that the imitative and social aspect of yoga may influence neural mechanism supporting aspects of social connectedness [48]. In line with this idea, one study evaluated whether plasma oxytocin—a neuropeptide implicated in aspects of social connection, recognition, and behavior [59]—changed as a result of yoga in patients with schizophrenia [39•]. Patients completing 1-month of yoga demonstrated increases in plasma oxytocin, while patients on a waitlist did not. That said, given the non-social nature of the comparison group, the effect of yoga on oxytocin may not have to do with yoga per se but simply increased social engagement, which could have been produced by other interventions with a social component. As mentioned, future studies examining social changes associated with yoga should be sure to include active interventions that control for this aspect of yoga.

In one other line of work, researchers have asked whether yoga affects neural mechanisms involved in synaptic plasticity, which may account in part for some of the positive cognitive changes observed in patients after yoga. One study evaluated this idea by examining the effect of yoga on brain-derived neurotrophic factor (BDNF) [38], a neutrotrophin that plays an important role in neurodevelopment, neurogenesis, and

[1] Assuming a small to medium effect size ($d$ = .40; Dauwan et al. [46••]) of yoga's effect on symptoms, functioning, or cognition, an $n$ = 100 per group would be needed to achieve power of .80 ($\alpha$ = .05, two-tailed).

synaptic plasticity [60]. Blood levels of BDNF are reduced in people with schizophrenia [60], which is thought to contribute to neurocognitive abnormalities associated with the disorder [61]. In a meta-analysis of schizophrenia subjects, higher level of BDNF expression was correlated to reasoning/problem solving [62••]. Furthermore, in post-mortem studies of schizophrenic subjects, measuring cortisol and BDNF levels in the brains revealed an inverse relationship; the lower the BDNF level, the higher was the cortisol level in prefrontal cortex and CSF samples [63]. BDNF levels have been shown to be malleable in response to behavioral interventions in schizophrenia [64•], as well as in response to yoga in patients with depression [65•]. However, in a study of yoga's effect on BDNF in patients, Ikai et al. [38] failed to find an effect of yoga on BDNF levels. The authors explain the null findings as a potential consequence of antipsychotic usage and the age of their sample, both of which affect BDNF levels.

It is known that stress and inflammation play a pivotal role in psychosis [66•]. Oxidative stress leads to inflammatory conditions which cause an increase in glucocorticoid levels or alterations in immune markers. In a meta-analysis, alterations in CSF levels of cytokines and tryptophan in schizophrenic patients were similar to the alterations in other psychiatric disorders such as major depressive disorder and bipolar disorder [67]. Reduction in inflammatory biomarkers such as cortisol, INL6 (interleukin 6), and TNF(tumor necrosis factor) was reported following yoga-based lifestyle intervention in chronic diseases such as diabetes and hypertension [68]. Preliminary evidence points toward some role of anti-inflammatory agents and antioxidants toward reducing positive and negative symptoms of schizophrenia in early stages—oxidative stress and neuroinflammation may serve as potential targets for developing newer drugs [52•, 69, 70]. If chronic inflammation is believed to be the cause of schizophrenia, yoga might help by reducing these inflammatory biomarkers.

Evidence of HPA (hypothalamo-pitutary-adrenal) axis abnormality suggests that alteration in this link causes increase in glucocorticoids leading to elevated cortisol levels. Neuroimaging findings in schizophrenia participants provide evidence of elevated dopamine levels in response to increased glucocorticoid secretion [71]. Conversely, a decrease in stress was related to lower cortisol and subsequently lower dopamine level in animal studies, a response similar to the action of antipsychotic medications [72]. Exercise has an effect in reducing stress as evidenced by decrease in cortisol and increase in B endorphins [72]. Yogasana, which is a type of physical exercise, can therefore be speculated to have a similar effect on cortisol release. In schizophrenic subjects, this would mean a decrease in dopamine level as well, thereby improving positive symptoms. In a study of yoga's effect on depression, yoga was said to increase the parasympathetic tone, thereby reducing the input of norepinephrine to hypothalamus, resulting in decreased secretion of cortisol. This relaxing effect was evident in the antidepressant and anxiolytic effects of yoga therapy [29]. That being said, a similar effect could be expected to be seen in schizophrenia participants with mood and anxiety symptoms.

Besides increasing inflammatory cytokines, allosteric stress can also reduce GABA levels, which in turn promotes depressed mood and increase in anxiety. Disruption in GABA levels is said to cause neuronal dysfunction, thereby affecting dopamine neurotransmission in psychosis [73•]. A 12-week trial of Iyengar yoga was linked with improved mood and anxiety, which correlated with increased GABA levels as evidenced by magnetic resonance spectroscopy [22]. Yet, another study also found that compared to an hour-long reading session and hour-long yoga session produced increases in GABA levels [74]. It is known that negative symptoms and cognitive deficits affect functional outcome in schizophrenia. Decrease in stress is believed to alter neuronal hormones and neural networks thereby improving neurocognition and social cognition [75••]. If GABA levels are believed to increase with reduction in allosteric stress, it is plausible that such alteration may improve affective symptoms and ultimately functional outcome in schizophrenic subjects.

## Conclusion

The available evidence suggests that yoga may positively impact aspects of the illness and may work through a variety of neurobiological mechanisms. Given initial evidence of efficacy, potential cost-effectiveness [76], and lack of adverse events [44•], the use of yoga as an adjunctive treatment is promising and deserving of additional *high quality* research. Researchers should also examine questions relating to dose and intensity of practice needed to affect change, various components of yoga practice, active ingredient of yoga's benefit, and neurobiological mechanisms. Although there exists no "standard treatment," the use of standardized, detailed, and freely available protocols would go a long way in helping move the field forward. We call for additional work in the form of preregistered, adequately powered, randomized controlled trials that include active control groups, assays of potential mechanisms, and follow-up assessments.

### Compliance with Ethical Standards

**Conflict of Interest** David Dodell-Feder, Annesly Gates, Dr. Donna Anthony, and Dr. Smita Agarkar declare that they have no conflicts of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance


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