THE EFFECTS OF YOGA ON COGNITIVE FUNCTION IN NEUROPSYCHIATRIC DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

Yoga has been increasingly utilized as a potential intervention to improve cognitive functioning in patients with neuropsychiatric disorders. However, evidence-based review is limited. Further, whether the observed yoga-related changes in cognitive function are systematically related to specific neuropsychological domains or specific neuropsychiatric disorders remains underexplored. Thus, the aim of this review is to systematically evaluate randomized controlled trials that objectively measure global cognitive function and/or other neuropsychological domains (e.g., attention, executive functioning, social cognition, and memory) in neuropsychiatric populations. Four broad clusters of neuropsychiatric disorder are discussed: focal neurobehavioral syndromes; major neuropsychiatric disorders; neurological conditions with cognitive, emotional, and behavioral features; and comorbid neuropsychiatric and neurological conditions.

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CHAPTER 1

INTRODUCTION

The number of yoga practitioners in the United States general population has significantly increased in recent years (Cramer et al., 2016). In a recent United States nationally representative survey, Cramer and colleagues (2016) reported adults' lifetime and 12-month prevalence of yoga use at about 31 million and 21 million, respectively. Yoga, derived from the Sanskrit root "yuj" or "to yoke" or "to unite" (Iyengar, 1965), functions to unify the mind and body through coordinated movement (asana), breath regulation (pranayama), and meditative practice (pratyahara, dharana, dhyana, samadhi) (Gard, Noggle, Park, Vago, & Wilson, 2014). As a practice thought to subserve soteriological outcomes (i.e., salvation from suffering) by "stilling the winds" of the mind (Jain, 2014), yoga has garnered significant attention for its potential to ameliorate disease-related suffering. Indeed, yoga practitioners report improved health, reduced stress, and disease prevention as primary motivators to engage in practice, suggesting that yoga is often perceived as a form of therapy to self-manage health-related concerns (Cramer et al., 2016). Importantly, the barriers to access are low and the diversity of practice styles and settings (e.g., at home, in gyms, outdoors) facilitates an adaptive, individualized practice (Balasubramaniam, Telles, & Doraiswamy, 2013). In addition to low barriers to access, preliminary evidence suggests that yoga may lead to symptom improvement in various neurological and psychiatric disorders (Balasubramaniam et al., 2013; Field, 2017; Gard et al., 2014; Mooventhan & Nivethitha, 2017). This positions yoga as a potentially viable intervention for a broad landscape of neuropsychiatric disorders and symptoms (Balasubramaniam et al., 2013). However, yoga has, since the

1970s, become increasingly popularized and corporatized (Balasubramaniam et al., 2013; Jain, 2014). While the "McYoga" model has increased society's access to and awareness of yoga, it has simultaneously diluted the quality of instruction and confused the messaging of the practice through consumer-driven hype and overstatement (Balasubramaniam et al., 2013). Consequently, yoga is a difficult system for medical professionals to confidently prescribe and for novice practitioners to assess; there is often difficulty parsing the legitimate therapeutic outcomes of the practice from cure-all claims (Balasubramaniam et al., 2013). To better elucidate some of the benefits, this work aims to systematically review and meta-analyze the available evidence analyzing yoga's effects on cognitive functioning in patients with neuropsychiatric disorders.

Neuropsychiatric disorders have a significant and often disabling impact on a large proportion of the human population (Taber, Hurley, & Yudofsky, 2010). Such disorders, including "organic" disorders that are primarily neurological in their presentation (e.g., Alzheimer's disease) and "functional" disorders, more often considered within the clinical province of psychiatry (e.g., schizophrenia), are among the leading causes of disability, accounting for approximately 20% of illness-related disability worldwide (Taber et al., 2010). The majority of disorders considered within the clinical purview of neuropsychiatry produce marked cognitive deficits (Miyoshi, Morimura, & Maeda, 2010). In fact, cognitive impairment is often considered a defining feature of neuropsychiatric disorders (Miyoshi et al., 2010). For example, memory is the primary cognitive deficit in Alzheimer's disease, whereas sustained attention is primarily disturbed in patients with attention-deficit/hyperactivity disorder (Trivedi, 2006). Other neuropsychiatric disorders such as schizophrenia are considered disorders of a more ubiquitous cognitive impairment with disturbances in several neuropsychological domains (Trivedi, 2006).

According to the Centers for Disease Control and Prevention (CDC), cognitive impairment affects more than 16 million individuals in the United States (CDC, 2011) and subsequently results in burdensome economic effects (CDC, 2011). Alzheimer's disease and related dementias, for example, are estimated to be the third most expensive disorders to treat in the United States (CDC, 2011). In 2010, the average Medicaid nursing facility expenditure per state for individuals with Alzheimer's disease was estimated at $647 million, excluding home- and community-based care or prescription drug costs (CDC, 2011). These high costs of care contribute to heavy demands placed on caregivers (CDC, 2011). In 2009, it was estimated that 12.5 billion hours of unpaid care was provided by more than 10 million family members caring for a person with cognitive impairment, valuing at $144 billion (CDC, 2011). Given these impacts on society as well as the individual, identifying novel interventions to improve cognitive functioning in patients with Alzheimer's disease and other neuropsychiatric disorders is an urgent public health priority.

Cognitive impairment is characterized by unexpected deficits in several cognitive processes or neuropsychological domains including attention (e.g., sustained attention, divided attention, selective attention, processing speed); executive function (e.g., planning, decision making, working memory, responding to feedback/error correction, overriding habits/inhibition, mental flexibility); learning and memory (e.g., immediate memory, recent memory, long-term memory); language (e.g., expressive language, receptive language); perceptual-motor (e.g., visual perception, visuo-constructional, perceptual-motor, praxis, gnosis); and social cognition (e.g., recognition of emotions, theory of mind) (Semrud-Clikeman & Ellison, 2009). Deficits might include significant differences in cognitive functioning from baseline measures, significant differences compared to healthy age-matched controls, or significant differences compared to the level of other neuropsychological domains in an individual (e.g., a deficit in attention with all other neuropsychological domains intact). These deficits, most reliably assessed using neuropsychological tests and batteries, are important to evaluate as cognitive functioning is often considered a strong predictor of functional outcome for patients with neuropsychiatric disorders (Trivedi, 2006). Therefore, special attention should be devoted to its assessment and management.

In recent years, there has been a burgeoning of research on potential pharmacological agents to target cognitive impairment in neuropsychiatric disorders (Wallace, Ballard, Pouzet, Riedel, & Wettstein, 2011). As reviewed by Wallace and colleagues (2011), drugs that enhance neurotransmission (e.g., acetylcholinesterase inhibitors), stimulate or inhibit key brain receptors (e.g., nicotinic agonists and 5-HT6 receptor antagonists) and activate intracellular signaling cascades (e.g., PDE inhibitors) are among some of the more promising pharmacological approaches for neuropsychiatric disorders. Presently, however, consensus is lacking on optimal disease-relevant drug targets (Wallace et al., 2011). Additionally, there are few or no viable treatment options for cognitive impairment associated with several neuropsychiatric disorders (e.g., schizophrenia) (Wallace et al., 2011). For example, while antipsychotic medication is effective in reducing the positive symptoms of schizophrenia, it is of less benefit for negative symptoms and cognitive deficits, which contribute most to disability (Broderick

& Vancampfort, 2017). While treatments targeting Alzheimer's disease are more robust and widely researched compared to other neuropsychiatric disorders, the current list of approved cognitive-enhancing drugs for Alzheimer's disease remains limited (Wallace et al., 2011). Additionally, approved drugs evidence only modest improvements in cognition and often produce troubling side effects (Wallace et al., 2011). Therefore, while existing pharmacological treatments confer some therapeutic benefit and have significant potential to improve the cognitive deficits observed across neuropsychiatric disorders, they are markedly limited at this point and not without adverse effects (Wallace et al., 2011). The side-effect profile of many drugs and the inherent limitations or lack thereof of medications for cognition have resulted in non-pharmacological interventions being utilized and researched as an adjunctive/alternative to pharmacotherapy in neuropsychiatric populations (Broderick & Vancampfort, 2017; Sachdeva, Kumar, & Anand, 2015).

Several non-pharmacological interventions evidence the potential to improve and preserve cognitive function in individuals with and without neuropsychiatric disorders (Sachdeva et al., 2015). These non-pharmacological interventions include physical exercise, sleep, yoga and meditation, spiritual practices, computer training, brain stimulation, and music (Sachdeva et al., 2015). Among these, Sachdeva and collages (2015) evidence the utility of physical activity/exercise, especially aerobic exercise, across different age groups and patient populations, including patient populations with or without cognitive impairment. Available evidence suggests that exercise benefits cognitive functioning in participants with mild cognitive impairment or early-stage dementia, Alzheimer's disease, Parkinson's disease, and depression and anxiety disorders

(Sachdeva et al., 2015). Specifically, aerobic exercise has evidenced improvements in several neuropsychological domains including memory, processing speed, attention, and executive functioning (Sachdeva et al., 2015). Yoga, a form of exercise, has similarly emerged as a promising intervention to improve cognition in subjects with psychiatric disorders (e.g., schizophrenia, depression), age-related cognitive decline, and degenerative disorders (Sachdeva et al., 2015). Though evidence is limited, yoga-related improvements have been reported in global cognition and several neuropsychological domains including immediate and delayed recall, verbal and visual memory, attention, working memory, verbal fluency, executive function, and processing speed for patients with and without cognitive decline (Sachdeva et al., 2015). Meta-analyzing chronic (long-term) and acute (immediate, single bouts) interventions in a diverse patient sample, Gothe and McAuley (2015) found that yoga produced moderate improvements in cognitive performance with the strongest effects for attention and processing speed, followed by executive function, and memory. Acute studies showed a stronger overall effect of yoga on cognition with the strongest effects on memory, followed by attention and processing speed measures, and executive function (Gothe & McAuley, 2015). In summary, there is preliminary support (albeit limited) for yoga's efficacy as adjunctive therapy for cognitive deficits; however, there has not yet been a systematic review assessing its utility in patients with a broad landscape of neuropsychiatric disorders.

The primary purpose of this meta-analysis review is to quantitatively assess the effects of yoga on cognitive function in neuropsychiatric disorders as measured by objective neuropsychological tests and batteries. Randomized controlled trials (RCTs) that objectively measure global cognitive function and/or specific neuropsychological domains (e.g., attention, memory, etc.) were reviewed. Better understanding of the effects of yoga on cognitive functioning has the potential to inform both appropriate interventional trials and clinical decision-making. In particular, this review aims to investigate how yoga impacts cognitive outcomes in four broad, but clinically distinct clusters of neuropsychiatric disorder: focal neurobehavioral syndromes; major neuropsychiatric disorders; neurological conditions with cognitive, emotional, and behavioral features; and comorbid neuropsychiatric and neurological conditions (Arciniegas & Kaufer, 2006). The following questions are addressed: (1) What is the effect of yoga on global cognitive function and/or other neuropsychological domains (e.g., attention and processing speed, executive function, memory, and social cognition) in neuropsychiatric disorders; and (2) To what extent is yoga's effects on cognitive function moderated by neuropsychiatric disorder?

Statement of the Problem

Currently, there is a lack of evidence-based review on the effects of yoga on cognitive functioning in patients with neuropsychiatric disorders. To provide well-rounded guidelines for the treatment of cognitive impairment in neuropsychiatric disorders, adjunctive therapies or complementary alternatives warrant strategic analysis. The development of a systematic review provides a sound framework by which to assess the overall effect of yoga on cognitive function in neuropsychiatric disorders. If basic assumptions are met, statistical analysis can be performed to evaluate the effectiveness of yoga on global cognitive function and/or specific neuropsychological domains across a broad landscape of neuropsychiatric disorders.

Research Questions

This meta-analysis was guided by the following research question: To what extent is yoga an effective intervention for cognitive impairment in patients with neuropsychiatric disorders? Sub-questions include: (1) What is the effect of yoga on global cognitive function and/or other specific neuropsychological domains (e.g., attention, executive function, memory, and social cognition) in neuropsychiatric disorders (2) To what extent is yoga's effects on cognitive function moderated by neuropsychiatric disorder?

Limitations

The following limitations are present in this meta-analysis:

1. One potential limitation is the high paucity of RCTs with strong methodological designs (Park et al., 2014). In yoga research, double blinding is neither practical nor possible as most people have received exposure, either directly or indirectly, to yoga practice (Gothe & McAuley, 2015). Because it is widely assumed that yoga confers health benefits, it is possible that participants ultimately report improvements because they expect to experience improvements; in other words, benefits may accrue through the placebo effect thereby confounding the findings (Gothe & McAuley, 2015). Additionally, several studies fail to report on blinding parameters of the assessors (Gothe & McAuley, 2015).

2. Another methodological limitation is the size and composition of treatment groups. Small sample sizes are common in yoga studies (Anand & Verma, 2014), thereby limiting the generalizability of the findings. The composition of samples is often homogeneous in terms of gender and demographics, which further limits the

generalizability of findings. For example, some studies only include female patients (Lin et al., 2015).

3. The variability of yoga protocols presents another limitation. Yoga is comprised of several components, rendering it an inherently difficult system to evaluate in clinical trials (Park et al., 2014). The yoga protocols employed in the studies included within this review will likely vary considerably in terms of style, structure, frequency, intensity, duration of practice sessions, location of practice, and total duration of training. Indeed, this variability limits the potential for generalizability. Additionally, the heterogeneity of yoga limits the ability to isolate the specific components (e.g., breath regulation, movement, and meditation) and/or external factors (e.g., social interaction) of the practice that confer salutary effects (Park et al., 2014).

4. An additional methodological limitation is the lack of adequate control conditions in RCTs evaluating the effects of yoga (Park et al., 2014). As Park and colleagues (2014) explain, determining a control condition is significantly more complex for behavioral interventions compared to pharmacological interventions. In their recent meta-analysis, Park et al.'s (2014) findings indicate that about half of the RCTs on yoga included only inactive waitlist or usual care control groups whereas the other half randomized participants to a more active treatment condition to control for a variety of specific or nonspecific effects. The authors only reported one RCT that used both an active and inactive control (Park et al., 2014). There are varying rationales for why a study might employ a passive versus an active control (Park et al., 2014). This review included RCTs that employed inactive and/or active control conditions as the extant literature does not offer empirical support for a particular control condition. As evidenced

in Park et al.'s review (2014), the literature is split on the control conditions for yoga studies. Inconsistent control conditions will likely be observed in this review and limit the interpretability of the findings.

5. Heterogeneity, or diversity, of the included studies will likely be high due to significant variability of yoga protocols, methodological inconsistencies, and diverse population characteristics (e.g., age, diagnosis, medication status, etc.).

6. High selection bias is a valid concern (Cramer, Langhorst, Dobos, & Lauche, 2015). Cramer and colleagues' (2015) meta-analysis determined that risk of selection bias was generally high in RCTs of yoga; however, the situation has improved since the publication of the revised CONSORT statement in 2001. The authors advise that pre-CONSORT RCTs and RCTs published in journals without impact factors be evaluated cautiously (Cramer et al., 2015).

Delimitations

The following delimitations are present in this meta-analysis:

1. Only studies that evaluate the effects of yoga on cognitive functioning in patients with neuropsychiatric disorders were included. Neuropsychiatric disorders included focal neurobehavioral syndromes; major neuropsychiatric disorders; neurological conditions with cognitive, emotional, and behavioral features; and comorbid neuropsychiatric and neurological conditions (Arciniegas & Kaufer, 2006).

2. Only studies which used objective and validated measures of global cognitive function and/or neuropsychological domains pre-and post-intervention and report mean change, standard deviation, and *p*-value statistics (or other adequate statistics from which to compute an effect) were eligible for inclusion.

3. Studies included were limited to RCTs, which are more methodologically sound and may be more heavily weighted in determining the quality of evidence regarding yoga's effects on cognitive functioning in neuropsychiatric disorders.

Definition of Key Terms

Attention. The ability to identify relevant stimuli, focus on relevant stimuli rather than others (selective attention), perform a task in the presence of distracting stimuli (focused attention), sustain focus on the stimulus until it is processed (sustained attention or vigilance), and allow for the transfer of the stimulus to higher-level processes (Semrud-Clikeman & Ellison, 2009; Trivedi, 2006).

Attention and processing speed. The capacity to focus and sustain attention in mental activity is reflected in processing speed, simple accuracy in a sustained focus task, divided thinking among tasks, mental manipulation and control, and resistance to internal or external distraction (Swiercinsky & Naugle, n.d.).

Continuous performance test. Tests that require intense attention to a visual-motor task to assess sustained attention and freedom from distractibility (Swiercinsky & Naugle, n.d.; Trivedi, 2006), such as the test of variables of attention (TOVA) (Braverman et al., 2010).

Control condition. In an experimental design, treatment is extended to the experimental or treatment group and withheld from the control condition (Gill & Walsh, 2010). Researchers investigating the effects of yoga most often employ a passive control condition, such as a waitlist or usual treatment group (Park et al., 2014). Increasingly, researchers have instead employed active control conditions, such as relaxation or exercise (Park et al., 2014). Very rarely, researchers employ both control conditions in yoga studies (Park et al., 2014).

Cognition. Broadly described as information processing, cognition is the acquisition of sensory information and the storage, retrieval, and use of that information for initiating behavioral decisions (Rowe & Healy, 2014; Trivedi, 2006). It includes processes of knowing, including attending, remembering, and reasoning, and also retaining the content of the processes, such as concepts and memories (American Psychological Association [APA], 2015). It denotes a relatively high level of processing of specific information including thinking, memory, perception, motivation, skilled movements, and language (Trivedi, 2006).

Cognitive processes. Constitute higher mental processes, such as perception, memory, language, problem solving, and abstract thinking (APA, 2015).

Cognitive (executive) control. The ability to synchronize thought and action and direct it toward goal attainment (Miller & Wallis, 2009). Involved in overcoming local or environmental challenges, planning and initiating complex sequences of behavior, and prioritizing goals (Miller & Wallis, 2009).

Cognitive impairment. Marked by difficulties in remembering information, learning novel tasks, attending to tasks, and initiating decisions necessary for everyday functioning, cognitive impairment ranges from mild cognitive impairment to severe cognitive impairment (e.g., Alzheimer's disease), with severe cognitive impairment resulting in the inability to initiate daily tasks of living and live independently (CDC, 2011). Cognitive impairment can be syndromic, occurring as a syndrome or part of a syndrome (e.g., mild cognitive impairment, subjective cognitive decline, mild neurocognitive disorder, or cognitive frailty), or etiologic, caused by an underlying etiology or pathology (e.g., prodromal Alzheimer's disease, early symptomatic Alzheimer's disease, or schizophrenia) (Morley et al., 2015). A variety of conditions, many of which are age-related, impair cognition (Morley et al., 2015) and may result in the inability to pay attention, process information quickly, remember and recall information, respond to information quickly, think critically, plan, organize and solve problems, and initiate speech and movement (Trivedi, 2006).

d2 Test of Attention. Measures selective attention and mental concentration (Bates & Lemay, 2004; Swiercinsky & Naugle, n.d.).

Executive function. Encompasses behaviors that are associated with skills in planning, cognitive flexibility, response inhibition, organization, and working memory thus enabling one to achieve insight and self-awareness (metacognition); to reflect on, initiate, evaluate, and regulate (activate and inhibit) thinking and behavior; to think flexibly; and to make decisions integrating judgment and feedback (Semrud-Clikeman & Ellison, 2009). Refers to the ability to use abstract concepts, to form an appropriate problem-solving test for the attainment of future goals, to plan one's actions, to develop strategies for problem-solving, and to execute these with the self-monitoring of one's mental and physical processes (Trivedi, 2006).

Heterogeneity. Any type of variability among studies included within a systematic review or meta-analysis (e.g., clinical, methodological, and statistical variability) (Higgins & Green, 2008). More conventionally, heterogeneity is interchangeable with statistical heterogeneity, which refers to the variability in intervention effects among the studies under review (Higgins & Green, 2008). Statistical heterogeneity arises when the intervention effects under study are more different from each other than one would expect due to random error (chance) alone (Higgins & Green, 2008).

Intelligence. A summary and multifaceted concept of general mental capability, reflecting the ability to comprehend, adapt to, and interact with the environment and also, profit from experience (APA, 2015). Intelligence is comprised of several domains. It is usually included in a neuropsychological assessment as a comprehensive functional index and, because it is multifaceted, may not reflect some forms of brain injury or disorder (Swiercinsky & Naugle, n.d.).

Language. The ability to receive and express thought through various forms of symbolic manipulation is measured in various language tests. Involves precepts that include spoken (expressive) and listening (receptive) aspects as well as the ability to name objects. Expressive language involves that which one uses to communicate to another person or to oneself. Receptive language is the ability to listen, comprehend, and appropriately form a response (APA, 2015).

Learning and memory. The acquisition of new information and retrieval of information for later use (Semrud-Clikeman & Ellison, 2009, p. 118). Learning suggests a relatively permanent change in behavior has occurred (APA, 2015) and is measured in verbal/auditory and in spatial/visual modalities (Swiercinsky & Naugle, n.d.).

Long-term memory. Memory processes associated with the preservation of information for retrieval at any later time (APA 2015). Not all information is converted into long-term memory; it depends on the content of the information as well as the goals of the individual (Swiercinsky & Naugle, n.d.).

Memory. The mental capacity to encode, store, and retrieve information (APA, 2015).

Includes sensory memory, short-term memory, working memory, and long-term memory (Semrud-Clikeman & Ellison, 2009).

Meta-analysis. A meta-analysis is simply "an analysis of analyses" (Glass, 1976, p. 3). More specifically, as defined by Carpenter (2017), a meta-analysis is the estimation of a population effect size by calculating a weighted estimate of that effect across all the obtainable studies of that effect. In other words, a meta-analysis summarizes the overall effect size of a particular treatment or intervention (Glass, 1976). In doing so, meta-analyses have the potential to provide more precise estimates of the effects of particular treatments or interventions compared to those derived from the individual studies included within a review (Higgins & Green, 2008).

Neuropsychiatry. Broadly described as "a medical specialty dedicated to the study of brain-behavior relationships of all manner and to the treatment of patients suffering from disturbances in these relationships" (Arciniegas & Beresford, 2001, p. 3).

Neurobehavioral and neuropsychiatric disorders. Defined as disorders of neurologically-based cognitive, emotional, or behavioral disturbances and classified into four broad, but clinically distinct subgroups as established by Arciniegas and Kaufer (2006): (1) focal neurobehavioral syndromes (e.g., aphasias, apraxias, agnosias, aprosodias, apathy, executive dysfunction, orbitofrontal syndrome); (2) major neuropsychiatric disorders (e.g., neurocognitive disorders and the major primary psychiatric disorders, including those with atypical or refractory presentations, etc.); (3) neurological conditions with cognitive, emotional, and behavioral features (e.g., dementias, movement disorders, stroke, epilepsy, multiple sclerosis, traumatic brain injury, neuroendocrine disorders, etc.); and (4) comorbid neuropsychiatric and neurological conditions (e.g., obsessive-compulsive disorder and Tourette's syndrome, Huntington's disease and alcohol abuse, etc.). For simplicity, the broad landscape of neurobehavioral and neuropsychiatric disorders is termed neuropsychiatric disorders.

Neuropsychological assessment. Comprehensively assesses a range of cognitive or neuropsychological domains, including, but not limited to, attention, intellectual or academic functioning, learning, memory, language, visuospatial reasoning, sensorimotor functioning, executive functioning, emotions, and psychopathology (Harvey, 2012; Kulas & Naugle, 2003).

Prefrontal cortex. Plays a central role in cognitive control, functioning to synthesize information to produce goal-directed behavior (Miller & Wallis, 2009). Involved in processes of inhibition, planning, working memory, evaluating consequences, and learning (Miller & Wallis, 2009).

Problem solving and judgment. Refers to advanced, higher-order information processing where knowledge is assessed and manipulated to find solutions to problems and make informed and reasoned judgments. Arithmetical thinking is a kind of problem solving (Swiercinsky & Naugle, n.d.).

Rey-Osterrieth Complex Figure Test (RCFT). Analyzes aspects of visuospatial ability and memory in all ages (Swiercinsky & Naugle, n.d.).

Ruff Figural Fluency Test (RFFT). A visual procedure that complements verbal fluency tests in assessing ability to think flexibly, but using visual stimuli rather than words (Swiercinsky & Naugle, n.d.).

Sensory memory. Constitutes the initial memory processes involved in the momentary preservation of fleeting impressions of sensory stimuli (i.e., when one is looking, hearing, or feeling something and processing it in milliseconds to seconds) (APA, 2015). Sensory memory is not stored; it is registered by the brain without processing (Semrud-Clikeman & Ellison, 2009).

Short-term memory. Information that is stored for just a few minutes and is not placed into permanent memory stores (Swiercinsky & Naugle, n.d.).

Social cognition. Includes a set of skills that enable one to understand the thoughts and intentions of others and respond appropriately to others' social actions (Lazar et al., 2014). It is considered to be a cognitive domain subserving the mental processes associated with social interactions (Roelofs, Wingbermühle, Egger, & Kessels, 2017).

Stroop Color and Word Test. A brief neuropsychological assessment of attention, mental speed, and mental control to assess executive functioning (Scarpina & Tagini, 2017; Swiercinsky & Naugle, n.d.; Trivedi, 2006).

Tower of London Test. Assesses higher-level problem-solving, valuable for examining executive functions and strategic planning (Swiercinsky & Naugle, n.d.).

Trail Making Tests A and B. Assesses attention, visual searching, mental processing speed, and the ability to mentally control simultaneous stimulus patterns (Swiercinsky & Naugle, n.d.). Trailing Making Test, part B, is a measure of executive function (Reitan, 1958; Trivedi, 2006).

Verbal (word) fluency tests. There are a variety of verbal fluency tests in use. Each is designed to measure the speed and flexibility of verbal thought processes (Swiercinsky & Naugle, n.d.).

Visuospatial ability. The ability to receive, interpret, and apply meaning to visual information as measured by constructional skills and visual perceptual tests. It is the capacity to make sense of the visual world - shapes, angles, larger gestalts vs details, the meaning of forms - and to reproduce what one sees (Swiercinsky & Naugle, n.d.).

Wechsler Adult Intelligence Scale – III. Includes 13 separate "subtests" to produce measures of memory, knowledge, problem solving, calculation, abstract thinking, spatial orientation, planning, and speed of mental processing. Performance on each subtest yields implications for different neurofunctional domains. Often, the WAIS-III is the foundation for a comprehensive neuropsychological assessment (Swiercinsky & Naugle, n.d.).

Wechsler Memory Scale – III. Includes 18 separate "subtests" to assess memory and learning capabilities. Provides a comprehensive assessment of memory. It is usually used in conjunction with the WAIS-III (Swiercinsky & Naugle, n.d.).

Working memory. The limited capacity memory system for the temporary storage and manipulation of information (e.g. verbal material, visuospatial images) (Pantelis & Maruff, 2002). Working memory is closely related to attention in that it involves keeping a limited amount of information active, frequently updated, and rapidly accessible for a brief time span. Most people have a working memory capacity of about seven items (e.g., a phone number) (Swiercinsky & Naugle, n.d.). Thought to be sustained by a network of temporary memory systems, it plays a crucial role in many cognitive tasks, such as reasoning, learning and understanding. It refers to the ability to hold the stimuli 'online' for a short time, then either use it directly after a short delay or process or manipulate it mentally to solve cognitive and behavioral tasks. Working memory seems to depend on the function of the prefrontal cortex (Trivedi, 2006).

Yoga. Derived from the Sanskrit root "yuj" or "to yoke" or "to unite" (Iyengar, 1965), yoga functions to unify the mind and body through coordinated movement (asana), breath regulation (pranayama), and meditative practice (pratyahara, dharana, dhyana, samadhi) (Gard et al., 2014). While there are several schools of yoga, Raja yoga and Hatha yoga (a derivative of Raja yoga) are most prevalent in Western modern practice (Gard et al., 2014). Raja yoga included several components or limbs (Gard et al., 2014) which, traditionally, are thought to subserve soteriological outcomes (i.e., salvation from suffering) (Jain, 2014). Briefly, the limbs are as follow: moral observances (ethics when interacting with others); self-discipline (ethics geared toward the self); physical postures and exercises; breath regulation; sensory withdrawal (minimizing sensory input); concentration (effortful, focused attention); meditation (effortless, unbroken flow of attention), and self-transcendence (see Gard et al., 2014). Modern postural yoga (MPY) is typically an amalgam of some meditative techniques, movement, breathing techniques, and philosophical and ethical teachings (Gard et al., 2014).

CHAPTER 2

LITERATURE REVIEW

Due to the wide scope of a systematic review, this literature review will be brief, but cover the critical components of this research.

Overview of Neuropsychiatry and Neuropsychiatric Disorders

Neuropsychiatry, according to Arciniegas and Beresford (2001), can be broadly defined as a field devoted to the "study of brain-behavior relationships of all manner and to the treatment of patients suffering from disturbances in these relationships" (p. 3). In accordance with Arciniegas and Beresford (2001), I subscribe to the philosophical position that "mental states are brain states" (p. 3). This position asserts that all disturbances of cognition, emotion, and/or behavior are the result of brain disturbances (Arciniegas & Beresford, 2001). Operating from this position, psychiatric disorders are thereby considered neurologic disorders (Arciniegas & Beresford, 2001). It is also recognized that neurologic disorders entail disturbances of cognition, emotion, and behavior, often referred to as neuropsychiatric symptoms (Arciniegas & Beresford, 2001; Miyoshi et al., 2010). As Arciniegas and Beresford (2001) argue, the attempt to parse psychiatric disorders and neurologic disorders into discrete categories has been largely arbitrary. Significant ambiguity regarding the etiology of these disorders impedes any definitive distinction (Arciniegas & Beresford, 2001). Important to this review, it is also increasingly recognized that there are limitations in studying the breadth of shared disturbances observed in psychiatric and neurologic patients (e.g., cognitive impairment) through a dichotomous framework (Arciniegas & Beresford, 2001). Such a framework might impede understanding of the presenting disturbance (e.g., cognitive impairment) and optimal treatment.

In an attempt to resolve the historical dichotomization of "psychiatric" versus "neurological" disorders, Arciniegas and Kaufer (2006) propose that clinical signs, symptoms, and syndromes supersede traditional methods of study (i.e., DSM-based classification) and instead, be considered as reflective of neural processes. Establishing this integrative approach transcends the traditional mind-brain duality, which is perpetuated through the dichotomization of psychiatry and neurology. Arciniegas and Kaufer (2006) propose a merging of these two disciplines into a single medical subspecialty: behavioral neurology and neuropsychiatry. As the authors detail, this subspecialty stresses deeper understanding of the links between neuroscience and behavior, including the treatment of individuals with neurologically-based behavioral disturbances (Arciniegas & Kaufer, 2006, p. 7). Other works support this paradigm shift and suggest that a broad landscape of disorders is appropriately subsumed under the neuropsychiatric disorder category (Miyoshi et al., 2010; Taber et al., 2010).

This systematic review was conducted using Arciniegas and Kaufer's (2006) proposed behavioral neurology and neuropsychiatry framework to allow for a broad screen of yoga's effects on neurological, cognitive, and psychiatric disorders that may either cause or are often associated with cognitive impairment. Neurobehavioral and neuropsychiatric disorders were broadly defined as disorders of neurologically-based cognitive, emotional, or behavioral disturbances and were classified into four broad, but clinically distinct subgroups, as established by Arciniegas and Kaufer (2006): (1) focal neurobehavioral syndromes (e.g., aphasias, apraxias, agnosias, aprosodias, apathy, executive dysfunction, orbitofrontal syndrome); (2) major neuropsychiatric disorders (e.g., neurocognitive disorders and the major primary psychiatric disorders, including those with atypical or refractory presentations, etc.); (3) neurological conditions with cognitive, emotional, and behavioral features (e.g., dementias, movement disorders, stroke, epilepsy, multiple sclerosis, traumatic brain injury, neuroendocrine disorders, etc.); and (4) comorbid neuropsychiatric and neurological conditions (e.g., Down's syndrome and Alzheimer's disease, obsessive-compulsive disorder and Tourette's syndrome, Huntington's disease and alcohol abuse, etc.). For simplicity, the broad landscape of neurobehavioral and neuropsychiatric disorders is referred to as neuropsychiatric disorders.

Yoga and its Utility for Neuropsychiatric Disorders

The number of yoga practitioners in the United States general population has significantly increased in recent years (Cramer et al., 2016). In a recent United States nationally representative survey, Cramer and colleagues (2016) reported adults' lifetime and 12-month prevalence of yoga use at about 31 million and 21 million, respectively, evidencing its popularity. Derived from the Sanskrit root "yuj" or "to yoke" or "to unite" (Iyengar, 1965), yoga functions to unify the mind and body through coordinated movement (asana), breath regulation (pranayama), and meditative practice (pratyahara, dharana, dhyana, samadhi) (Gard et al., 2014). While there are several schools of yoga, Raja yoga and Hatha yoga (a derivative of Raja yoga) are most prevalent in Western modern practice (Gard et al., 2014). Raja yoga includes several components or limbs, including moral observances (ethics when interacting with others); self-discipline (ethics geared toward the self); physical postures and exercises; breath regulation; sensory withdrawal (minimizing sensory input); concentration (effortful, focused attention); meditation (effortless, unbroken flow of attention), and self-transcendence (Gard et al., 2014). These limbs provide several self-regulatory strategies ultimately designed to still the dysfunctional thoughts and ruminations of the mind (i.e., the source of suffering), thereby encouraging mind-brain-body wholeness and wellness (Iyengar, 1965). MPY practices are typically an amalgam of some meditative or concentrative exercises, movement, breathing techniques, and philosophical and ethical teachings, thus providing the practitioner with an expanse of techniques thought to promote overall health and well-being (Gard et al., 2014).

As a practice thought to subserve soteriological outcomes (i.e., salvation from suffering) by "stilling the winds" of the mind (Jain, 2014), yoga has garnered significant attention for its potential to ameliorate disease-related suffering. As a result, there has been a surge of publications on yoga to mitigate disease-related symptoms in clinical populations (Jeter, Slutsky, Singh, & Khalsa, 2015). Indeed, yoga practitioners consistently report improved health, reduced stress, and disease prevention/management as primary motivators to engage in practice, suggesting that yoga is widely perceived as a form of therapy to self-manage health-related concerns (Cramer et al., 2016). To explore psychiatric inpatients' motivations to engage in practice, Sistig, Lambrecht, and Friedman (2015) utilized semi-structured interviews and weekly journal entries. Similar motivational themes emerged; patients reported that yoga increased relaxation, reduced stress, improved energy, enhanced the ability to focus, and increased motivation to engage in life (Sistig et al., 2015). Additional evidence suggests that psychiatric patients are receptive to the use of complementary and alternative medicine (CAM) therapies

(Elkins, Rajab, & Marcus, 2005). Among CAM therapies (Park, 2013), response to yoga has been generally positive in patients with schizophrenia spectrum disorders (Govindaraj, Varambally, & Gangadhar, 2015; Sistig et al., 2015). For example, in Bhatia et al.'s (2016) research, participants told the yoga teacher that yoga made them more active. Paikkatt et al. (2015) received similar confirmation. Initially, the research team had difficulty getting the patients to cooperate and participate in yoga therapies; however, once exposed to the training, patients were largely in favor of yoga after only one week of practice. In fact, patients were found waiting in the ward with proper dress and were encouraging other inpatients to practice. Anecdotal reports in Visceglia and Lewis' (2011) study offers additional reports. Patients reported positive changes: "yoga makes me feel like my whole body is functioning as it should"; "calming myself down"; "I thought it would require a lot out of me, but instead it has given me so much." Some reported using the deep breathing techniques as coping strategies outside of the practice. Physicians also reported that patients were calmer, less aggressive, and functioning better. Two patients were reported to be more adherent to medications and treatment interventions. Fewer additional medications for acute agitation were noted for one patient and one patient reported to be "better able to control impulses and refrain from acting out" (Visceglia & Lewis, 2011). These anecdotal results are encouraging to the potential use of yoga as an adjunctive therapy. As these publications demonstrate, practitioners often perceive improvements in mental health and well-being in response to yoga. This suggests that the practice is generally well-received, which hints at its potential utility in populations where mental states are disturbed.

In addition to being well-received, the barriers to practice are low and the diversity of practice styles and settings (e.g., at home, in gyms, outdoors) facilitates an adaptive, highly individualized practice (Balasubramaniam et al., 2013). Further, adverse effects are relatively rare in the literature, suggesting yoga is well-tolerated in neuropsychiatric populations. While there are some case study reports describing adverse outcomes, including the exacerbation of psychotic symptoms (Lu & Pierre, 2007), these reports are rare. Other publications have further detailed some of the untoward effects of yoga, including complications arising from intermediate to advanced poses (e.g., inversions), hot yoga classes, and rapid cycling breathing (Anand & Verma, 2014; Brown & Gerbarg, 2005; Mooventhan & Nivethitha, 2017). Other reviewers have suggested that there is a lack of information regarding yoga's adverse effects, thus impeding any recommendation regarding its add-on utility (Cramer, Lauche, Klose, Langhorst, & Dobos, 2013; Krisanaprakornkit, Ngamjarus, Witoonchart, & Piyavhatkul, 2010). In general, however, preliminary evidence widely suggests that yoga is a safe, adjunctive form of therapy for symptom improvement in various neurological and psychiatric disorders (Anand & Verma, 2014; Balasubramaniam et al., 2013; Field, 2017; Mooventhan & Nivethitha, 2017; Rao, Varambally, & Gangadhar, 2013).

Yoga has been proposed as a viable adjunctive therapy for a broad landscape of neuropsychiatric disorders, including schizophrenia spectrum disorders (Dodell-Feder, Gates, Anthony, & Agarkar, 2017; Gangadhar & Varambally, 2012); multiple sclerosis (Anand & Verma, 2014; Field, 2017); major depressive disorder (Anand & Verma, 2014; Rao et al., 2013; Gangadhar & Varambally, 2012); attention-deficit/hyperactivity disorder (Balasubramaniam et al., 2013); and generalized anxiety disorder (Anand & Verma, 2014). Reviewing yoga's utility for neurological disorders, Mooventhan and

Nivethitha (2017) suggest that yoga is a potential effective adjuvant for patients with various neurological disorders including stroke, Parkinson's disease, multiple sclerosis, epilepsy, Alzheimer's disease, dementia, headache, myelopathy, and neuropathies. Balasubramaniam and colleagues (2013), in their systematic review of yoga for psychiatric disorders, further substantiate yoga's adjunctive potential for schizophrenia and attention-deficit/hyperactivity disorder and also, in managing depressive symptoms. Similarly, Rao et al.'s (2013) review of the literature demonstrates yoga's efficacy as a therapy for depressive disorders as well as the negative and cognitive symptoms of schizophrenia. Dodell-Feder et al. (2017) further evidence the positive effects of yoga on the symptomatology of schizophrenia, particularly in the negative and cognitive symptom domain, and also, promote its stress-regulating potential. Gangadhar & Varambally (2012) lend additional support to Dodell-Feder et al.'s (2017) conclusions, demonstrating the feasibility and efficacy of yoga as adjunctive therapy in schizophrenia, again in the negative and cognitive symptom domains. Though promising conclusions have been drawn, there is lack of consensus in the literature regarding yoga's adjunctive utility for neuropsychiatric disorders.

Several systematic reviews have produced inconclusive findings regarding yoga's utility as an add-on therapy for schizophrenia (Broderick & Vancampfort, 2017; Cramer et al., 2013; Krisanaprakornkit et al., 2010). In their systematic review of the evidence, Broderick and Vancampfort (2017) found that while there may be some minor improvements in quality of life in favor of yoga as an add-on therapy, there was insufficient evidence to make any robust claims regarding its utility as an add-on to standard care packages for schizophrenia. Details are fully reported in their Cochrane review (Broderick & Vancampfort, 2017). Further, Cramer et al. (2013) systematically reviewed the effects of yoga on symptoms of schizophrenia, quality of life, function, and hospitalization in patients with schizophrenia, finding only moderate evidence for short-term effects of yoga on quality of life. These effects, however, were not clearly distinguishable from bias, and safety of yoga interventions remained unclear; therefore, the researchers could not recommend yoga as a routine intervention for schizophrenia (Cramer et al., 2013). Systematically reviewing yoga's efficacy for patients with multiple sclerosis, Cramer and colleagues (2014) concluded that lack of methodologically sound evidence impeded any recommendation of yoga as a routine intervention for patients with multiple sclerosis. For attention-deficit/hyperactivity disorder, similar inconclusive findings were reported by Krisanaprakornkit et al. (2010) in their Cochrane review. Owing to the limited number of included studies, the small sample sizes, the high risk of bias, and the unclear adverse effects, the researchers were unable to draw any conclusions regarding the effectiveness of meditation therapy for attention-deficit/hyperactivity disorder (Krisanaprakornkit et al., 2010).

Taken together, several lines of evidence propose yoga as a potential viable intervention for a broad landscape of neuropsychiatric disorders; however, more recent, high-quality systematic reviews indicate a scarcity of evidence from which to draw such claims. The available research, limited by small sample size, few randomized studies, inadequate control conditions, diverse yoga protocols, limited assessments, and lack of safety data, thus precludes any firm conclusions on the efficacy of adjunctive yoga for neuropsychiatric disorders (Anand & Verma, 2014). Therefore, in light of inconsistent findings and methodological limitations, evidence in support of add-on yoga therapies must be interpreted cautiously. However, as pointed out by Keshavan, Rao, and Rao (2013), such limitations are not unique to yoga research, but are instead a theme of any burgeoning field of research that aims to develop novel therapeutic interventions. Given yoga's broad public appeal, its low barriers to access, and its relative non-invasiveness as compared to other neuropsychiatric therapies, it is of considerable potential for large scale dissemination, even if effects are modest (Keshavan et al., 2013). For this reason, methodologically rigorous studies evaluating its effects are warranted to move the field forward and to more decisively determine the validity of applying yoga as a mainstream therapeutic add-on for neuropsychiatric disorders (Keshavan et al., 2013).

Cognition, Disruptions, and Assessment

In the philosophical domain of cognitive science, several scholars and theorists have recognized the disclarity and deficiency of extant definitions of cognition (Buckner, 2015; Heersmink, 2017). While there are several prominent definitions, this review adopts Rowe and Healy's (2014) definition, which broadly describes cognition as information processing (p. 1288). Expanded, cognition is the acquisition of sensory information and the storage, retrieval, and use of that information for initiating behavioral decisions (Rowe & Healy, 2014). Importantly, the maintenance of cognition is key to good health, successful aging, and quality of life (Morley et al., 2015). Disruption in cognition at any level of severity has the potential to create burdensome effects for both individuals and their caregivers (Morley et al., 2015).

According to the CDC (2011), more than 16 million people in the United States are living with cognitive impairment. Characterized by difficulties remembering information, learning novel tasks, attending to tasks, and initiating decisions necessary for everyday functioning, cognitive impairment exists on a spectrum, ranging from mild cognitive impairment to severe cognitive impairment (e.g., Alzheimer's disease), with severe cognitive impairment resulting in the inability to initiate daily tasks of living and live independently (CDC, 2011). Ranging in presentation, individuals might report several functional deficits: difficulties with multiple stimuli; becoming easily distracted; the inability to perform mental calculations; the inability to do complex projects; expending extra effort to organize; exhaustion during social gatherings; repeating self in conversation; requiring frequent reminders; using general phrases (e.g., "that thing on your foot") rather than the name of an object (i.e., "shoe"); trouble remembering names of family members; trouble with previous familiar activities; trouble navigating familiar environments; trouble with spatial tasks; atypical behavior outside of the acceptable social range; insensitivity to social standards; and unsafe decision-making behavior. As Morley and colleagues (2015) detail, cognitive impairment can be syndromic, occurring as a syndrome or part of a syndrome (e.g., mild cognitive impairment, subjective cognitive decline, mild neurocognitive disorder, or cognitive frailty), or etiologic, caused by an underlying etiology or pathology (e.g., prodromal Alzheimer's disease, early symptomatic Alzheimer's disease, schizophrenia, attention-deficit/hyperactivity disorder).

With the "Baby Boomer" generation passing the age of 65, the number of people living with cognitive impairment is expected to increase significantly (Alzheimer's Association, 2016; CDC, 2011). In 2011, an estimated 5.1 million Americans aged 65 years or older were living with Alzheimer's disease, the most florid manifestation of cognitive impairment; this number is predicted to rise to 13.2 million by 2050

(Alzheimer's Association, 2016; CDC, 2011). After the age of 70, several studies suggest that approximately 16% of persons have subthreshold cognitive impairment or mild cognitive impairment and 14% experience dementia (CDC, 2011). Approximately two-thirds of persons with dementia identified in population studies have Alzheimer disease, either alone or with comorbidities (CDC, 2011). While age is the greatest risk factor for cognitive impairment, cognitive impairment is not confined to aging populations or certain disease (CDC, 2011; Morley et al., 2015). Disrupted cognition is a hallmark feature of several neuropsychiatric disorders (Kulas & Naugle, 2003). Discussion of the various manifestations and disease-relevant presentations of cognitive impairment is beyond the scope of this review; however, it is important to highlight that almost all neuropsychiatric disorders are intermingled with disruptions in cognition if evaluated closely (Miyoshi et al., 2010). Cognitive impairment, then, is not pathognomonic to a certain neuropsychiatric disorder, but spans several diagnostic categories.

Disruptions in cognitive function, for example, are well-documented in multiple sclerosis, an autoimmune disorder. Occurring in about 40-65% of patients, disruptions in memory, attention and information processing speed, executive function, mental flexibility, intelligence, and visuo-construction are particularly evident (Winkelmann, Engel, Apel, & Zettl, 2007). Several neuropsychiatric disorders associated with cognitive impairment are common in multiple sclerosis, even in the early stages of the disease (Paparrigopoulos, Ferentinos, Kouzoupis, Koutsis, & Papadimitriou, 2010). Major depression is the most common comorbid neuropsychiatric disorder with an approximate 50% lifetime prevalence (Paparrigopoulos et al., 2010). According to Paparrigopoulos et al. (2010) and Miyoshi et al. (2010), symptoms of apathy and depression have been closely associated with higher levels of cognitive impairment in multiple sclerosis. Multiple sclerosis with comorbid major depression is also a strong predictor of morbidity, mortality, patient quality of life, and possibly disease progression; it has also been found to correlate with the caregiver's distress and quality of life (Paparrigopoulos et al., 2010). Mild cognitive impairment and dementia are also relatively prevalent in multiple sclerosis (Westervelt, 2015). Various other neuropsychiatric symptoms and disorders, such bipolar disorder, fatigue and sleep disorders, anxiety, euphoria, psychosis, and personality changes occur in patients with multiple sclerosis (Paparrigopoulos et al., 2010). These neuropsychiatric symptoms and disorders are often associated with higher levels of cognitive impairment (Paparrigopoulos et al., 2010). These varying degrees of impairment whether arising from multiple sclerosis or multiple sclerosis-related neuropsychiatric manifestations have major impacts on functional outcomes, especially socio-occupational functioning and quality of life, even in patients with multiple sclerosis who have minimal physical disability (Winkelmann et al., 2007). These neuropsychiatric symptoms and disorders, arising from "organic" brain disorders, are similarly common in other disorders including epilepsy, Parkinson's disease, and are very much intermingled with cognitive impairment (Sahakian et al., 2015).

Several psychiatric disorders are also intermingled with various disruptions of cognitive function including schizophrenia (Barch, 2005; Konstantakopoulos et al., 2011; Pantelis & Maruff, 2002; Rund & Borg, 1999; Stuchlik & Sumiyoshi, 2014); obsessive-compulsive disorder (OCD) (Stuchlik & Sumiyoshi, 2014; Trivedi, 2006); major depressive disorder (Austin, Mitchell, & Goodwin, 2001; Trivedi, 2006); bipolar disorder (Trivedi, 2006); attention-deficit hyperactivity disorder (Trivedi, 2006); borderline personality disorder (Trivedi, 2006); substance use disorder (Trivedi, 2006); and somatic symptom disorders (Trivedi, 2006). Schizophrenia, one of the most debilitating psychiatric disorders, has long been recognized as a disorder of significant cognitive abnormality with interruptions in several cognitive domains including, but not limited to, attention, working memory, executive control, and episodic memory (Barch, 2005; Rund & Borg, 1999). In fact, schizophrenia has often been considered, at its core, a cognitive disorder; more specifically, it has been proposed as a higher-order attentional deficit disorder (Rund & Borg, 1999). Indeed, several lines of evidence support its status as a cognitive disorder (Barch, 2005; Pantelis & Maruff, 2002; Rund & Borg, 1999; Stuchlik & Sumiyoshi, 2014). Further, cognitive deficits are strongly predictive of quality of life, daily functioning, and patients' long-term outcome (Barch, 2005). There is also a strong association between cognitive dysfunction and social deficits (Rund & Borg, 1999). More recently, research has focused on social cognition in schizophrenia, specifically facial emotion recognition deficits (FERD) (Behere et al., 2011; Behere, 2015). Social cognitive deficits, common in other neuropsychiatric disorders, are of clinical importance as research has demonstrated this cognitive domain is predictive of socio-occupational functioning (Lazar, Evans, Myers, Moreno-De Luca, & Moore, 2014; Roelof et al., 2016).

To assess these cognitive deficits, a neuropsychological assessment is performed (Harvey, 2012; Kulas & Naugle, 2003). Neuropsychological assessments are typically comprehensive and cover a range of cognitive domains including, but not limited to, attention, intellectual functioning, learning, memory, language, visuospatial reasoning, sensorimotor functioning, executive functioning, emotions, and psychopathology

(Harvey, 2012; Kulas & Naugle, 2003). The neuropsychological domains of interest in this systematic review are as follows: attention and processing speed, memory, executive functioning, and social cognition. Depression is also assessed as a secondary outcome measure. There are several validated tests to measure these domains of cognition and affective states. For a list of commonly administered tests, see Appendix E.

Yoga and Cognitive Functioning

Yoga has emerged as a potential intervention to improve cognition in subjects with psychiatric disorders, age-related cognitive decline, and degenerative disorders (Balasubramanian et al., 2013; Sachdeva et al., 2015). Several recent reviews and meta-analysis publications have comprehensively examined the effects of yoga on cognitive functioning in patients with and without neuropsychiatric disorders (Acevedo et al., 2016; Balasubramaniam et al., 2013; Clark, Schumann, & Mostofsky, 2015; Field, 2017; Gard et al., 2014; Gothe & McAuley, 2015; Luu & Hall, 2016; Rao et al., 2013; Sachdeva et al., 2015). Though evidence is limited, yoga-related improvements have been reported in general cognition and several neuropsychological domains including immediate and delayed recall, verbal and visual memory, attention, working memory, verbal fluency, executive function, and processing speed for patients with and without cognitive impairment (Acevedo, Pospos, & Lavretsky, 2016; Sachdeva et al., 2015). Acevedo et al.'s (2016) review suggests that meditative practice influences brain systems involved in attention, awareness, memory, sensory integration, and the cognitive regulation of emotion. Through these underlying mechanisms, Acevedo et al. (2016) suggest that meditative practice might confer brain health benefits for aging adults for social cognition, attention, memory, and emotional regulation that can help in preventing mood, physical, and cognitive disorders of aging. Reviewing the therapeutic potential of yoga for psychiatric disorders, Rao et al. (2013) suggest yoga as a potential treatment to improve the cognitive deficits commonly observed in schizophrenia, specifically social cognition deficits. To summarize the effects of Hatha yoga on executive function, Luu and Hall (2016) conducted a systematic review of experimental studies; of the 11 published studies eligible for inclusion, at least half evidenced significant improvements in executive function following Hatha yoga. These improvements were observed in healthy adults, children, adolescents, healthy older adults, impulsive prisoners, and other medical populations (with the exception of multiple sclerosis) (Luu & Hall, 2016). Meta-analyzing chronic (long-term yoga interventions) and acute (immediate, single bouts) in a diverse patient sample, Gothe and McAuley (2015) found that yoga produced moderate improvements in cognitive performance with the strongest effects for attention and processing speed, followed by executive function, and memory. Findings evidenced a stronger overall effect on cognition following acute exposure with the strongest effects on memory, followed by attention and processing speed measures, and executive function (Gothe & McAuley, 2015). While findings lend modest support to the cognitive-enhancing utility of yoga, the literature is fraught with inconsistencies and methodological limitations, as previously discussed. For example, Balasubramaniam et al. (2013) systematically reviewed the evidence for yoga's efficacy in the treatment of major psychiatric disorders, concluding that RCTs in cognitive disorders yielded conflicting results.

Taken together, preliminary evidence suggests yoga's utility to improve cognitive functioning across several diagnostic lines; however, there is a lack of good-quality evidence from which to draw any definitive conclusion. Importantly, there is lack of systematic evaluation regarding the adjunctive therapeutic potential of yoga for cognitive deficits in patients presenting with a broad landscape of neuropsychiatric disorders.

Yoga and Cognition: Identifying Putative Mechanisms

Preliminary evidence suggests that yoga and its components serve to improve cognitive deficits (Clark et al., 2015; Gard et al., 2014; Gothe & McAuley, 2015; Singh, Goel, Kathrotia, & Patil, 2014). Although these cognitive-enhancing effects have been observed in the literature (albeit scarcely and tentatively), the mechanisms by which yoga might improve cognition remain unclear. Several theories, some more heuristic than others, have attempted to explain the physiological and psychological mechanisms that subserve the yoga-related cognitive improvements often observed (Clark et al., 2015; Gard et al., 2014; Gothe & McAuley, 2015; Singh et al., 2014).

Attention

Attention plays a central role in yoga and is related to the construct of mindfulness (Pradhan, 2015). As Gard et al. (2014) explain, mindfulness practices are primarily cognitive, functioning to still mental chatter, promote self-awareness, and increase attention. To assess the link between cognitive function and mindfulness, Brunner, Abramovitch, and Etherton (2017) implemented a 6-week Hatha yoga program in healthy participants. Findings indicated significant improvement in working memory (manipulation and maintenance), consistent with Gothe and McAuley's (2015) earlier findings indicative of yoga-related improvements in executive function. Further, improvements in attentive mindfulness accompanied these cognitive gains (Brunner et al., 2017). These findings suggest that yoga, with its active mindfulness component, incurs cognitive benefits in several cognitive domains related to improvements in mindfulness, including attention (Brunner et al., 2017). In their review, Clark et al. (2015) further demonstrate how mindful movement can generate improvements in cognition, specifically attention, by developing the transferable skill of mindfulness.

Attention-Affect Interplay

Additionally, several studies have investigated the interplay of attention and affect in response to yoga and meditative practices (Gootjes, Franken, & Van Strien, 2011; Mackenzie et al., 2014; Menezes, Dalpiaz, Rossi, & De Oliveira, 2015; Tang, Posner, & Rothbart, 2014). Tang et al. (2014), for example, found significant improvement in executive attention in response to a form of meditation accompanied by self-reported improvements in mood compared to an active control condition (i.e., relaxation). In a study of female cancer survivors, Mackenzie et al. (2014) demonstrated that yoga was associated with an increase in associative attention and positive affective valence (e.g., calm, energy), concluding that yoga promotes “a confluence of associative attention and positive affect that effectively stills the changing states of the mind via heightened attention to the breath and body” (p. 143). Further, Menezes et al. (2015) assessed negative emotion interference during a high-attentional demand and a low-attentional demand condition as well as state and trait anxiety scores in yoga practitioners. Yoga practitioners, compared to non-practitioners, showed lower emotion interference in the high attentional condition, compared to the low attentional condition, perceived emotional images as less unpleasant, and reported lower state and trait anxiety. Also, emotion interference in the low attentional condition was lower amongst advanced practitioners, and state anxiety was lower amongst practitioners attending more than two weekly yoga classes. The results demonstrate that yoga, especially a sustained practice, may improve self-regulatory skills and reduce aversive emotional states (Menezes et al., 2015), thereby conferring cognitive benefits. Both studies suggest that yoga is a promising system subserving attention-affect regulation.

In a review of dialectical behavioral therapy, of which mindfulness is a core component, Lynch et al. (2006) propose that mindfulness, by regulating the cognitive domain of attention, likely functions to attenuate or eliminate secondary emotional responses, behavioral response tendencies, and/or cognitive appraisals that normally would generate suffering. It is suggested, based on empirical evidence, that mindfulness might alter default response tendencies by teaching practitioners to observe, identify, describe, and participate in emotional experiences rather than react to or act on negative affective states (Lynch et al., 2006). In this way, mindfulness may change not only the behavioral response to emotions, but also the associated thoughts (schemas), images, and/or memories (Singh et al., 2014). By changing dysfunctional default responses, mindfulness may reverse affect-biased responses that contribute to cognitive difficulties.

These suggestions align with the hypothetico-integrative model of yoga and meditation (Singh et al., 2014). Following Beck's psychopathology of the dysfunctional self, Singh et al. (2014) propose that yoga and meditation function to correct a biased dysfunction self through non-judgemental awareness or bare attention (e.g., perception without interpretation). A dysfunctional self, according to the authors, arises from "habitually biased information processing" (p. 23) that consequently distorts the individual's construction of experience, leading to a variety of cognitive errors, affect dysregulation, and inappropriate behavior. In accordance with Beck's model, it is argued that these distorted interpretations and perceptions are negatively reinforced by past dysfunctional beliefs incorporated into relatively persistent attention networks or schemas (Singh et al., 2014). This affect-biased attention is thought to influence and maintain disordered affective states. As Singh et al. (2014) demonstrate, yoga and meditative processes have the potential to correct affect-biased deficits through training and modulation of attentional networks (Singh et al., 2014). They propose that yoga and meditation interventions operate at all three levels of organization of the brain: the central nervous system (CNS), the autonomic nervous system (ANS), and the peripheral nervous system (PNS), resulting in sensory block, motor attenuation, and cognitive restructuring (Singh et al., 2014). They further propose that a consistent yoga and meditation practice may facilitate sustained improvement in the self-regulation of cognitions, emotions, and behaviors through the process of neuroplasticity and the functions of the anterior cingulate cortex (ACC), a region in the brain implicated in emotion regulation (Singh et al., 2014).

Singh et al.'s (2014) mechanistic explanation is consistent with and subsumed under Gard et al.'s (2014) self-regulatory model of yoga. Gard and colleagues (2014) present evidence that bottom-up and top-down self-regulatory processes in yoga may contribute to self-regulation across cognitive, emotional, behavioral, and physiological domains. Their proposed framework and systems network model integrates a great deal of theory and research. They further evidence yoga's potential to regulate emotion. Reviewing empirical evidence, the authors suggest that yoga and meditative practices might improve emotion regulation by (1) cultivating greater emotional awareness; (2) instructing skills to cognitively reappraise emotional stimuli; and/or (3) decreasing physiological indicators of stress thus changing psychophysiological reactivity to interoceptive threat, possibly depending upon affective context (Gard et al., 2014).

Overall, the mechanisms by which yoga affects cognition are not well understood, but there are many hypotheses that propose yoga might attenuate negative affective states thereby improving cognitive deficits; however, the reverse has also been suggested with yoga enhancing cognition thereby improving affect (Gard et al., 2014). Indeed, the distinction between emotion and cognition is a slippery one (Pessoa, 2015). Pessoa (2015) offers a thoughtful exploration into the ways by which emotion and cognition interact and are integrated in the brain, suggesting that research is ill-served by the dichotomization of concepts such as cognition and emotion. It is highly likely that a confluence of biological and psychological factors interplay to improve both emotional and cognitive deficits. Yoga might improve self-regulation abnormalities (i.e, affect dysregulation) through its self-regulatory components (e.g., mindfulness training), thereby strengthening the self-regulation of attention, which in turn, promotes improvements in controlling and coping with affect dysregulation, identity disturbance, and dysregulated behavior, including disinhibition tendencies, thereby allowing for enhanced cognitive control.

Neurobiological Explanations

Studies investigating the neural mechanisms of yoga and meditative practices evidence yoga's potential to improve brain networks relevant to the self-regulation of attention and affect (Acevedo et al., 2016; Boccia, Piccardi, & Guariglia, 2015; Froeliger, Garland, Modlin, & McClernon, 2012; Muehsam et al., 2017; Tang et al., 2014). A review of these findings is beyond the scope of this paper. Briefly, yoga has been found to enhance resting state activation across multiple cortico-striatal neuronal loops, a system thought to subserve executive functioning, and for which alterations have been associated with a host of neuropsychiatric disorders (Brunner et al., 2017). In a 2015 meta-analysis of fMRI studies, Boccia and colleagues found that brain areas from the occipital to the frontal lobes showed increased activation during meditation. This network included areas involved in processing self-relevant information (precuneus), processing self-regulation, focused problem-solving and adaptive behavior (ACC), interoception and in monitoring internal body states (insula), reorienting attention (angular gyrus), and processing the "experiential enactive self" (premotor cortex and superior frontal gyrus) (Boccia et al., 2015). Tang et al. (2014) found greater activation of the ACC and functional connectivity improvements observed between the ACC and striatum in subjects who meditated. Further, diffusion tensor imaging revealed that several white matter tracts connecting the ACC to other areas had improved their efficiency. Froeliger et al. (2012) investigated the effects of yoga on emotion-cognition interactions using an emotional Stroop test. Results indicated that practitioners showed greater ventrolateral prefrontal cortex (related to cognitive control of emotional distractions) activation when negative distractors were present compared to non-practitioners (Froeliger et al., 2012). According to Froeliger et al. (2012), this suggests that the yoga group was more engaged in the cognitive relevant task despite emotional interference, again pointing to yoga's attention-enhancing utility.

In summary, the highly focused attention during yoga combined with sustained posture, breath regulation, and meditation techniques are proposed to facilitate top-down and bottom-up mechanisms involving high-level cognitive networks and low level autonomic, interoceptive networks (Gard et al., 2014). By integrating these mechanisms, yoga has the potential to confer self-regulation improvements, including affect regulation (Gard et al., 2014). In light of the neurobiological findings, it is proposed that yoga will induce changes in neural pathways underlying self-regulation deficits, including the amygdala, ACC, and prefrontal cortex. Yoga might also result in changes in bottom-up pathways resulting in changes in insula activation, a critical region involved in interoceptive awareness (Gard et al., 2014). Taken together, it is proposed that by altering the neural connectivity related to the self-regulation of attention and emotion, yoga will confer cognitive improvements (Tang et al., 2014).

Meta-Analysis

Meta-analyses, a subset of systematic review, are the most frequently cited form of clinical research (Haidich, 2010). In fact, in the hierarchy of evidence, where clinical evidence is ranked according to the absence of various biases that afflict medical or evidence-based research, meta-analyses outrank all other study designs (Haidich, 2010). The process of conducting and reporting a high-quality meta-analysis progresses through a series of systematic steps of which have been detailed extensively (Haidich, 2010). This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009). The PRISMA Statement consists of a 27-item checklist and a four-phase flow diagram (Liberati et al., 2009). The checklist and flow diagram, as detailed by Liberati and colleagues (2009), was followed to ensure the transparency, complete reporting, and replicability of the review process (see Appendix A).

The usefulness of a meta-analysis occurs, according to Rousseau and Evans (2017), when (1) there is a need to resolve disagreement regarding the true effect size of a particular treatment or intervention in the literature and/or (2) to determine the assumptions that will be used when designing study hypotheses. The results of a meta-analysis can improve precision of estimates of effect, address questions not posed by the individual studies, settle inconsistencies in the literature, and produce new hypotheses (Rousseau & Evans, 2017). The purpose of this meta-analysis is to resolve the inconsistencies in the literature regarding the precise effect size of yoga on cognitive function in patients with neuropsychiatric disorders and, if practical, purport a potential mechanism by which yoga produces this effect. Additionally, the lack of meta-analyses on the effects of yoga on cognitive function in neuropsychiatric disorders warrants this review and quantitative analysis. To date, only one meta-analysis has evaluated the effects of yoga on cognitive function in patients with neuropsychiatric disorders; however, that particular study was not limited to neuropsychiatric disorders as it included a range of medical diagnoses (Gothe & McAuley, 2015). Thus, the aim of this meta-analysis is to determine whether a positive effect of yoga practice on cognitive function exists; and, ideally, to obtain a single summary estimate of the effect on global cognitive function and/or other neuropsychological domains of which include attention, executive function, memory, and social cognition. The additional aim is to perform a subgroup analysis (Borenstein & Higgins, 2013) to determine the effects of yoga on particular neuropsychiatric disorders (e.g., schizophrenia) or cerebral disorders with clinical manifestations of neuropsychiatric disorders (e.g., multiple sclerosis). Finally, if feasible, studies which included measures of cognitive function and affect will be analyzed to determine the mediating effects of emotion on cognitive outcomes. This is motivated by previous research that has posited an interplay between cognition and emotion, specifically the potential interplay of attention and affect (Marvel & Paradiso, 2004; Mathersul & Rosenbaum, 2016; Pessoa, 2015).

The meta-analytic approach necessitates several considerations (Haidich, 2010). Arguably, the most important consideration when conducting a meta-analysis is the evaluation of statistical heterogeneity (Haidich, 2010; Higgins & Thompson, 2002). Given the nature of yoga research, in which studies are typically conducted under different protocols and in different parts of the world as well as the variability of neuropsychiatric disorders and cognitive measures, the effect across studies will likely be heterogeneous (Park et al., 2014). Therefore, a random effects models, which operates under the assumption that a distribution of effects exists above that expected by chance, was used (Haidich, 2010; Higgins & Thompson, 2002). However, a random effects model does not facilitate comparisons of heterogeneity across studies of different types of outcomes, such as continuous outcomes (Higgins & Thompson, 2002). Because continuous data were meta-analyzed, it was important to measure the extent to which heterogeneity was present among studies (Higgins & Thompson, 2002). Assessing heterogeneity is commonly achieved using I^2, a statistic developed by Higgins and Thompson (2002), which quantifies the percentage of variability in point estimates that is due to heterogeneity rather than sampling error (Haidich, 2010). As Haidich (2010) advises, findings must be interpreted with caution when statistical heterogeneity is present. Further, researchers must implement methods to investigate potential sources of heterogeneity (Haidich, 2010). One such way to investigate potential reasons for heterogeneity is to conduct a subgroup analysis (Borenstein & Higgins, 2013). This approach groups categories of subjects (e.g., by diagnosis, age, sex, etc.) to compare effect sizes (Haidich, 2010). In this meta-analysis, a subgroup analysis was performed by diagnosis to elucidate potential sources of heterogeneity, and also, determine the differential effects of yoga on cognitive function across neuropsychiatric disorders.

An additional consideration when performing any meta-analysis is bias detection (Haidich, 2010; Rousseau & Evans, 2017). The most significant source of potential bias in meta-analyses results from the selection criteria used to identify the publications for inclusion (Dickersin, 2006; Haidich, 2010; Rothstein, Sutton, & Borenstein, 2006; Rousseau & Evans, 2017). Several methods have been developed to reduce the risk of publication bias or, at the very least, to inform the extent to which the meta-analysis accounts for publication bias; the most commonly used method is the funnel plot (Haidich, 2010; Rousseau & Evans, 2017). Developed by Light and Pillemer (1984), the funnel plot provides a graphical representation (i.e., a scatterplot) of each included study's effect estimates against its sample size (Egger, Smith, Schneider, & Minder, 1997). If publication bias is not detected, the plot is expected to have a symmetric inverted funnel shape (Egger et al., 1997). To evaluate evidence of publication bias in this meta-analysis, a funnel plots was used. However, as Egger and colleagues (1997) establish, funnel plots might be limited when meta-analyses are based on a limited number of small trials. This is of valid concern in this review as the scope of yoga research on cognition is limited, and often, yoga studies typically include small sample sizes (Gothe & McCauley, 2015; Park et al., 2014). As advised, the results from such analyses were interpreted with caution (Egger et al., 1997). Other sources of bias (e.g., lag time bias, selective reporting, and language bias) are also important to identify (Haidich, 2010); such biases were critically examined.

A conceptual question when conducting a meta-analysis is as follows: How many studies does one need to do a meta-analysis? There is no rule per se regarding the number of studies required. Valentine, Pigott, and Rothstein (2010), in their primer on statistical power for meta-analyses, concluded that, generally, the minimum requirement is two studies. Ideally, more studies would be included for higher statistical power, but when there is need to determine the effectiveness of a given treatment or intervention, conducting a meta-analysis on two studies is a superior analytic strategy compared to alternative methods (Valentine et al., 2010).

CHAPTER 3

METHODOLOGY

The objective of this study is to systematically review and meta-analyze RCTs evaluating the effects of yoga on cognitive function in patients with neuropsychiatric disorders. This chapter includes: (1) Research Design; (2) Inclusion of Studies; (3) Procedures; and (4) Statistical Analyses.

Research Design

This review was conducted following PRISMA guidelines for systematic reviews and meta-analyses (Liberati et al., 2009). The PRISMA statement is a 27-item checklist that aims to improve reporting of systematic reviews and meta-analyses (Liberati et al., 2009; see Appendix A). A detailed search strategy was conducted by a medical librarian. Inclusion criteria were defined a priori using the PICOS components (participants, interventions, comparators, outcomes, and study design) as defined by the PRISMA statement on systematic reviews (Liberati et al., 2009). Studies retrieved using the search strategy were screened in a blinded process by two independent authors, myself included, using Rayyan software, a tool designed to expedite the initial screening of abstracts and titles (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016), to identify studies that potentially satisfied the inclusion criteria. Any discrepancies over the inclusion of particular studies were resolved by a third reviewer. Prior to data extraction, two authors independently assessed the risk of bias using the Cochrane Risk of Bias Tool (RoB 2.0) for assessing the risk of bias in randomized trials (National Collaborating Centre for Methods and Tools, 2017; Page, Higgins, Clayton, Sterne, & Hrobjartsson, 2016). This tool assesses the following five domains: bias arising from the randomization process;

bias due to deviations from intended interventions; bias due to missing outcome data; bias in measurement of the outcome; bias in selection of the reported result (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). Risk of bias was assessed for each criterion as low risk of bias, unclear, or high risk of bias (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). Discrepancies were discussed with a third reviewer until a consensus was reached. A form, developed a priori, was used to extract data from the included studies for assessment of study quality and evidence synthesis. The protocol of this study was registered at the International Prospective Register of Systematic Review, PROSPERO, as is recommended in the methods section of the PRISMA checklist (Liberati et al., 2009), under the identification CRD42018087214 and can be accessed online (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018087214).

Inclusion Criteria

These were defined a priori using the PICOS components (participants, interventions, comparators, outcomes, and study design) as defined by the PRISMA statement on systematic reviews (Liberati et al., 2009).

Participants

Patients with a neuropsychiatric disorder were considered for inclusion. Four broad clusters of neuropsychiatric disorder were included: focal neurobehavioral syndromes; major neuropsychiatric disorders; neurological conditions with cognitive, emotional, and behavioral features; and comorbid neuropsychiatric and neurological conditions. No other restrictions regarding age or other population characteristics were applied. Any recognized diagnostic assessment of neuropsychiatric disorder was accepted.

Types of Interventions

Studies on yoga interventions must have included at least one of the following yoga components to be eligible: asana (physical postures), pranayama (breath control), mindfulness or meditation, and/or lifestyle advice (based on yoga philosophy and/or traditional yoga practices); these techniques have been shown through previous research to have potential influence on cognitive function (Acevedo et al., 2016; Balasubramaniam et al., 2013; Clark et al., 2015; Field, 2017; Gard et al., 2014; Gothe & McAuley, 2015; Luu & Hall, 2016; Rao et al., 2013; Sachdeva et al., 2015). No restrictions were imposed regarding yoga tradition, length, frequency or duration of the program. Studies on multimodal interventions, such as mindfulness-based stress reduction and mindfulness-based cognitive therapy, that include yoga amongst other practices, were excluded. Studies allowing individual co-interventions were eligible. No restrictions were made based on treatment setting or format of treatment. Studies comparing yoga to active (e.g., other exercise interventions, cognitive enhancement training) and/or non-active control conditions (e.g., treatment as usual, waitlist, conventional pharmacotherapy) were eligible.

Outcome Measures

The outcome measure for this study was the overall effect size of yoga on global cognitive function and neuropsychological domains across studies as computed by the Hedge's *g* statistic. To be eligible, RCTs must have assessed at least one or more objective assessments of cognitive functioning including global cognitive function and/or a specific neuropsychological domain (e.g., memory, attention, language, verbal fluency, visuospatial ability, social cognition, or executive function). All validated neuropsychological tests were accepted as measures of cognitive function. Studies that did not include a validated screening measurement scale for cognitive function or cognitive subdomains, such as the Hopkins Verbal Learning Test–Revised (HVLT-R) (Shapiro, Benedict, Schretlen, & Brandt, 1999), Rey-Osterrieth Complex Test (Rey-O) (Shin, Park, Park, Seol, & Kwon, 2006), Stroop Word and Color Test (Scarpina & Tagini, 2017), Trail Making Tests A and B, and Ruff Figural Fluency Test (RFFT), were excluded. In addition to the use of a validated test to assess cognition, studies must have reported statistical data from which to compute the Hedge's *g* statistic; this includes, but is not limited to, reported mean change, standard deviation, and *p*-value statistics.

Secondary outcomes included:

1. Subjective measures of mood, as measured by the Hamilton Rating Scale for Depression (HRSD-24 item) (Hamilton, 1960), the Calgary Depression Scale (CDS) (Addington, Addington, Maticka-Tyndale, & Joyce, 1992; Addington, Addington, & Maticka-Tyndale, 1994), or any other validated scale.
2. Safety of the intervention, as assessed by the number of adverse events.
3. Qualitative adherence data.

Types of Studies

Only RCTS (published and peer-reviewed) were considered for inclusion. No language restrictions or publication date restrictions were imposed on the initial search; however, studies without available data or without English translation were excluded.

Procedures

To identify studies included or considered, the reviewers worked with a medical librarian to develop a detailed search strategy for each database. These strategies were based on a search strategy developed for PubMed (NLM) that went through several iterations and was translated for each specific database (see Appendix B). The search strategies used a combination of controlled vocabulary and free text terms. Multiple search terms were used for cognitive impairment, disorders with known cognitive impairment (e.g., schizophrenia and other related disorders) combined with search terms for yoga. There were no date restrictions. The following electronic databases and grey literature sources were searched: (1) PubMed (NLM); (2) Embase (Elsevier); (3) Scopus (Elsevier); (4) Cochrane Central (Wiley); (5) PsycInfo (EbscoHost); (6) ClinicalTrials.gov; and (7) American Psychiatric Association (APA). After studies were identified, duplicate studies were omitted from the results. Endnote was used for the deduplication of records. Included studies were screened by title and abstract by two independent reviewers based on inclusion criteria. Rayyan QCRI was used to expedite the initial blinded screening of abstracts and titles by two independent reviewers, including myself (TJ) and NH (Ouzzani et al., 2016). If a decision could not be made regarding an article's eligibility, a third reviewer (CT) was called in to resolve discrepancies. The same two reviewers (TJ, NH) conducted a risk of bias assessment on included studies using the Cochrane Risk of Bias Tool (RoB 2.0) for assessing the risk of bias in randomized trials (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). This assessment evaluates the following: bias arising from the randomization process; bias due to deviations from intended interventions; bias due to missing outcome data; bias in measurement of the outcomes; bias in selection of the reported result (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). Risk of bias was assessed for each criterion as low risk of bias, some concerns, or high risk of bias (National Collaborating Centre for Methods and Tools, 2017; Page et al., 2016). The overall judgement of each item for each study was judged as 'low', 'high' and 'unclear' according to the levels of bias. Discrepancies between reviewers were resolved by the third reviewer (CT).

Data was extracted using a data extraction form created a priori. Cognitive tests used in all studies were classified into four categories: (1) attention and processing speed, which is the capacity to focus and sustain attention in mental activity is reflected in processing speed, simple accuracy in a sustained focus task, divided thinking among tasks, mental manipulation and control, and resistance to internal or external distraction (Swiercinsky & Naugle, n.d.); (2) executive function, which is the ability to use abstract concepts to form an appropriate problem-solving test for the attainment of future goals, to plan one's actions, to develop strategies for problem-solving, and to execute these with the self-monitoring of one's mental and physical processes (Trivedi, 2006); (3) memory, which involves the mental capacity to encode, store, and retrieve information (APA, 2015); and (4) social cognition, which includes a set of skills that enable one to understand the thoughts and intentions of others and respond appropriately to others' social actions (Lazar et al., 2014; Roelofs et al., 2017).

Statistical Analyses

All meta-analytic procedures were performed in version 3 of the meta-analysis software "Comprehensive Meta-Analysis" (CMA) (Borenstein, Hedges, & Higgins, 2005). The intervention effect of yoga was measured by Hedge's *g*, calculated in CMA from mean ± standard deviation and *p*-value statistics of pre- and post-test scores. Because most of the studies used multiple cognitive tests, often spanning each of the four cognitive domains, the following computations were performed: (1) an overall effect size for cognition; (2) an average effect size for each of the four cognitive domains; and (3) effect sizes by subgroup or diagnosis (Borenstein & Higgins, 2013). Study-specific effect size estimates were weighted by the study sample size and combined to form the overall study effect size. Forest plots were constructed to display overall effect sizes for the included studies. All effect sizes were coded such that positive numbers always reflected improvements in performance, and negative numbers reflected deterioration in performance. Several studies assessed score changes at multiple time points (Behere et al., 2011; Eyre et al., 2017; Lin et al., 2015). For simplicity, the mean of the time points was pooled. According to the Cochrane Collaboration handbook for systematic reviews of interventions, the choice between fixed or random effects meta-analysis should be based on the underlying "true" effect of an intervention on an outcome measure (Higgins & Green, 2011). Because the target populations, cognitive outcomes measures, and yoga interventions varied significantly across studies, a random-effects analysis was conducted to provide a conservative estimate of treatment effects (Borenstein, Hedges, Higgins, & Rothstein, 2010). Heterogeneity of treatment effects was assessed using the I^2 statistic. Significance level was set at $p < .05$ and confidence intervals, at 95%.

CHAPTER 4

RESULTS

Study Identification

Database and reference searches identified 1,126 studies for consideration. Two reviewers (TJ, NH) disregarded obviously irrelevant records based on the abstract or the title using Rayyan software (Ouzzani et al., 2016). After applying the inclusion criteria, a total of 27 potential studies were further evaluated for their eligibility. Twelve studies ultimately satisfied the inclusion criteria; however, two studies were excluded because they did not provide data and/or were not available in English (Beik, Nezakatalhoseini, Abedi, & Badami, 2015; Haffner, Roos, Goldstein, Parzer, & Resch, 2006). In the end, 10 studies involving 767 participants with neuropsychiatric disorders were included in the qualitative synthesis (Behere et al., 2011; Bhatia et al., 2016; Eyre et al., 2016; Eyre et al., 2017; Jensen & Kelly, 2004; Jayaram et al., 2013; Lin et al., 2015; Oken et al., 2004; Sharma, Das, Mondal, Goswami, & Gandhi, 2006; Velikonja et al., 2010). Four studies were subsequently excluded from the quantitative synthesis as they did not provide sufficient data from which to compute Hedge's *g* (Bhatia et al., 2016; Jensen & Kelly, 2004; Oken et al., 2004; Velikonja et al., 2010). Because of the scarcity of studies satisfying the inclusion criteria and insufficient data reporting, a mixed methods analysis of the results was adopted for a more comprehensive purview of the effects of yoga on cognition in neuropsychiatric disorders. The detailed screening of eligible studies is presented in Appendix C.

Characteristics of Included Studies

The characteristics of each of the included studies are summarized in Appendix D. Ten RCTs involving 767 participants with a diagnosed neuropsychiatric disorder (male 326, female 421, and 20 unspecified) with mean age 40.67 were included for review (Behere et al., 2011; Bhatia et al., 2016; Eyre et al., 2016; Eyre et al., 2017; Jensen & Kelly, 2004; Jayaram et al., 2013; Lin et al., 2015; Oken et al., 2004; Sharma et al., 2006; Velikonja et al., 2010). Studies were conducted in India (Behere et al., 2011; Bhatia et al., 2016; Jayaram et al., 2013; Sharma et al., 2006), America (Eyre et al., 2016; Eyre et al., 2017; Oken et al., 2004), China (Lin et al., 2015), Slovenia (Velikonja et al., 2010), and Australia (Jensen & Kelly, 2004). Neuropsychiatric disorders studied included schizophrenia spectrum disorders (Behere et al., 2011; Bhatia et al., 2016; Jayaram et al., 2013; Lin et al., 2015), mild cognitive impairment (Eyre et al., 2016; Eyre et al., 2017), multiple sclerosis (Oken et al., 2004; Velikonja et al., 2010), attention deficit-hyperactivity disorder (Jensen & Kelly, 2004), and major depressive disorder (Sharma et al., 2006). Participants were most often recruited from inpatient and/or outpatient clinics (Behere et al., 2011; Bhatia et al., 2016; Eyre et al., 2016; Eyre et al., 2017; Jayaram et al., 2013; Sharma et al., 2006), mental health service programs (Lin et al., 2015), and local advertisement initiatives (Oken et al., 2004). All included studies reported clear diagnostic, inclusion, and exclusion criteria for their participants. The yoga and meditation protocols implemented across studies were highly variable. Yoga styles employed were as follows: Hatha Yoga (Velikonja et al., 2010); Iyengar Yoga (Oken et al., 2004); Kundalini Yoga with Kirtan Kriya meditation (Eyre et al., 2016; Eyre et al., 2017); Sajah Yoga meditation (Sharma et al., 2006); and an integrated yoga therapy module developed by Swami Vivekananda Yoga Anusandhana Samsthana (SVYASA) (Behere et al., 2011; Jayaram et al., 2013). One protocol was unspecified (Lin et al., 2015). The frequency, practice time per session, and duration of intervention were largely inconsistent across studies. Frequency of practice varied from one weekly session to daily sessions; total practice time per session ranged from 12 minutes to one hour; and the duration of the intervention ranged from eight weeks to six months with either supervised training, home practice, and/or a combination of supervised training and home practice. Of these 10 studies, four exclusively compared yoga to an active control condition (e.g., physical exercise, memory enhancement training, cooperative games) (Eyre et al., 2016; Eyre et al., 2017; Jensen & Kelly, 2004; Velikonja et al., 2010); two compared yoga practice to a non-active control condition (e.g., conventional medication treatment, waitlist) (Jayaram et al., 2013; Sharma et al., 2006); and four compared yoga practice to both an active and non-active control condition (Behere et al., 2011; Bhatia et al., 2016; Lin et al., 2015; Oken et al., 2004). A wide variety of neuropsychological tools were implemented as listed in Appendix E. Different tools were applied to evaluate the same cognitive domain within and across studies.

Risk of Bias of Included Studies

Figure 1 provides a summary of the risk of bias of included studies. All included studies reported that groups were randomized, but only six of the studies described the method by which the randomization sequence generation was achieved. Such studies reported that randomization was achieved via a random number generator on a computer (Behere et al., 2011; Eyre et al., 2016; Eyre et al., 2017; Lin et al., 2015); an online randomization program (Bhatia et al., 2016); or a modified minimization scheme performed by a statistician who was otherwise uninvolved with the assessments (Oken et al., 2004). Four studies clearly reported allocation concealment as follows: Eyre et al. (2016; 2017) specifically stated that all groups were concealed as "wellness and mental stimulation" following computer generated randomization; Bhatia et al. (2016) reported that randomization lists were stored in a password protected computer by a study member who did not collect outcome measures, administer any interventions, or treat the participants; Lin et al. (2015) stated that allocation was concealed from research staff involved in assessment; and Oken et al. (2004) reported that randomization was exclusively performed by a project statistician who was otherwise uninvolved with the assessments. As evidenced in Figure 2, the risk of potential performance bias was high for all included studies due to the nature of the behavioral interventions assessed; it is impossible to blind participants to the status of their intervention and difficult to blind personnel and staff (e.g., yoga, exercise instructors, psychiatrists, psychologists, etc.). Six studies explicitly reported that outcome assessors were blinded; therefore, risk of detection bias was judged as low (Behere et al., 2011; Bhatia et al., 2016; Eyre et al., 2016; Eyre et al., 2017; Lin et al., 2015; Oken et al., 2004). The risk of attrition bias was low in five studies because the data were complete, or the number of missing data were detailed and explained (Bhatia et al., 2016; Eyre et al., 2016; Eyre et al., 2017; Lin et al., 2015; Oken et al., 2004). The selective reporting bias in four was judged as unclear as the authors provided incomplete data from which to compute an effect size (Bhatia et al., 2016; Oken et al., 2004; Jensen & Kelly, 2004; Velikonja et al., 2010). The risk of other bias was judged as high in one study due to limited sample size, confounds resulting from the crossover design, and potential uncontrolled placebo effects due to the 4:1 difference in contact time between the actively treated and control group (Jensen & Kelly, 2004). Similarly, other bias was judged as high in another study because of small sample size and lack of data for baseline characteristics between the intervention and control group, including information regarding sample size distributions (Velikonja et al., 2010). Following inspection of the funnel plot, publication bias was judged as low as most studies are plotted near the average with minimal asymmetry (see Figure 3); this, however, should be interpreted with caution due to reporting bias, including selective outcome reporting, selective analysis reporting, and language bias.

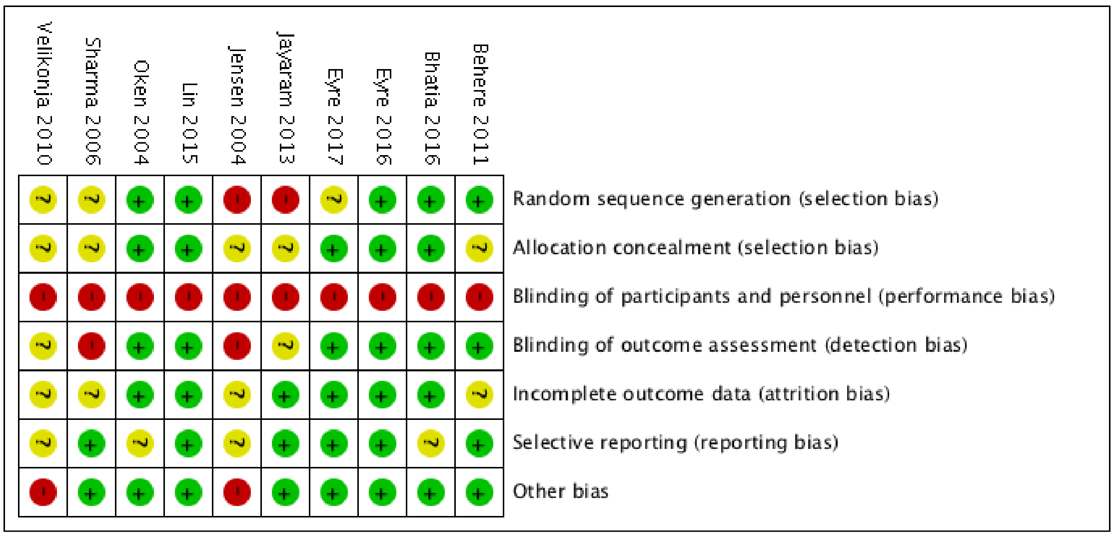

Figure 1. Risk of Bias Summary

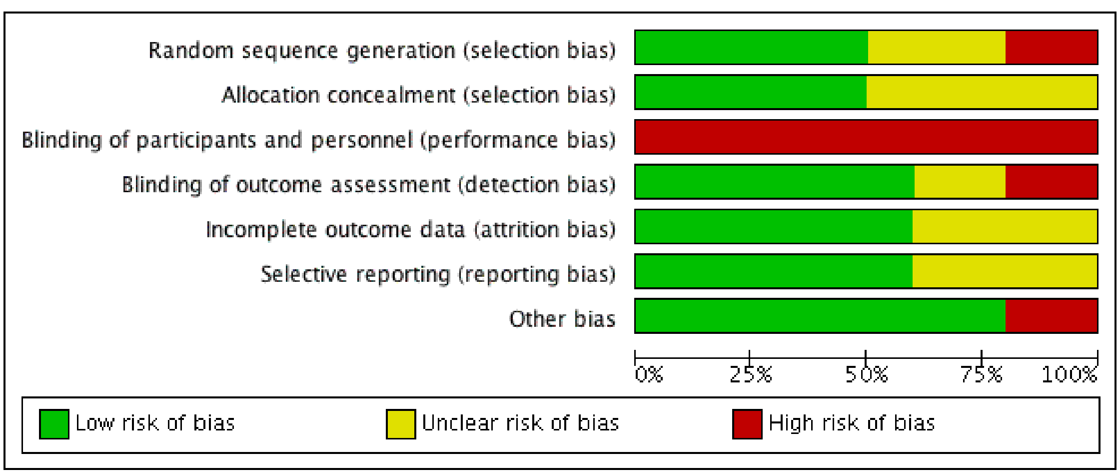

Figure 2. Risk of Bias Graph

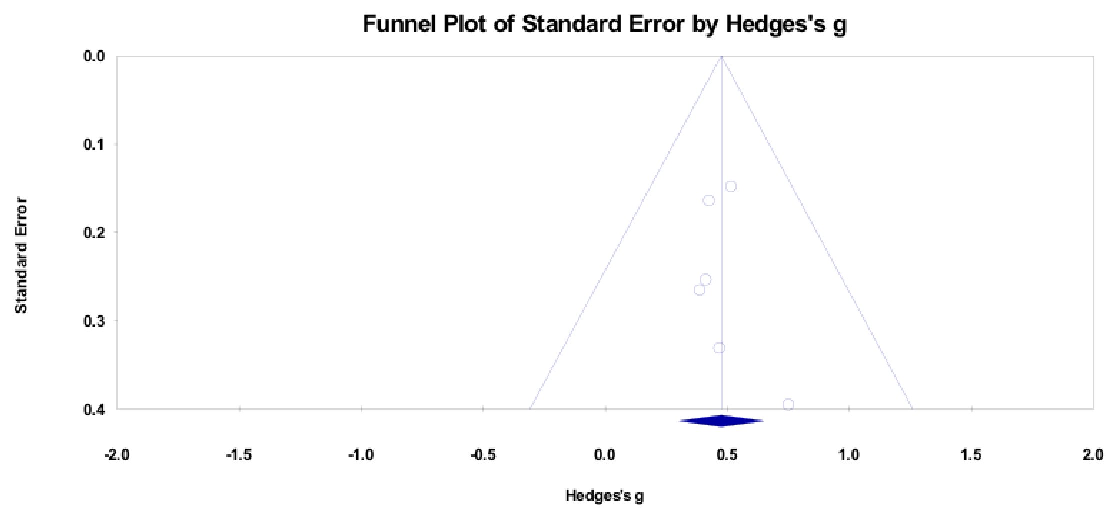

Figure 3. Funnel Plot of Standard Error by Hedge's *g*

Effects of Yoga Interventions

In the following sections, the effects of the yoga intervention on global cognitive function and neuropsychological domains are evidenced. Effects by diagnosis and secondary outcomes are also presented.

Global Cognitive Function

Of the six studies included in the quantitative synthesis, not one study administered a test to assess global cognitive ability. Overall effect sizes for studies involving 147 participants were thus calculated before examining specific neuropsychological domains as a generalization of yoga's overall effect on global cognitive function. A significant modest effect was found, g = .475 (SE =0.089, 95% CI =0.301–.649, p = .000, I^2 = 0%, the random-effects model; Figure 4). These findings must be interpreted cautiously owing to potential publication biases as detailed.

Overall Effect

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Behere et al., 2011	0.392	0.266	0.071	-0.131	0.914	1.470	0.142
Eyre et al., 2016	0.472	0.332	0.110	-0.179	1.123	1.421	0.155
Eyre et al., 2017	0.430	0.165	0.027	0.107	0.753	2.609	0.009
Jayaram et al., 2013	0.754	0.396	0.157	-0.022	1.531	1.904	0.057
Lin et al., 2015	0.520	0.149	0.022	0.228	0.812	3.494	0.000
Sharma et al., 2006	0.416	0.255	0.065	-0.083	0.915	1.633	0.103
	0.475	0.089	0.008	0.301	0.649	5.354	0.000

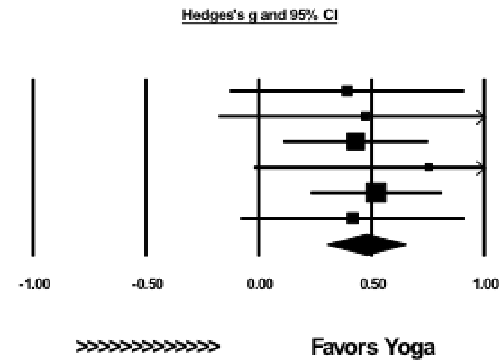

Figure 4. Overall Effect of Yoga on Cognitive Function

Social Cognition

Of the studies included in the quantitative synthesis, two studies with a total of 42 participants examined the effects of yoga on social cognition by assessing facial emotion recognition deficits (FERD) as measured by the Tool for Recognition of Emotions in Neuropsychiatric Disorders (TRENDS) (Behere et al., 2011; Jayaram et al., 2013). TRENDS performance was assessed by calculating the total number of images that were correctly identified out of a maximum of 80, termed the TRENDS Accuracy Score (TRACS) (Behere et al., 2008). A significant modest effect was found, g = .505 (SE = .221, 95% CI = .071-.938, p = .022, I^2 = 0%, the random-effects model; Figure 5). Bhatia and colleagues (2016) similarly assessed a measure of social cognition, emotion processing, using the University of Pennsylvania Computerized Neurocognitive Battery (Penn CNB) (Gur et al., 2001). While insufficient data was available to compute an effect size, the authors reported significant yoga-related improvements on emotion processing for the speed index of the Penn CNB, thus lending additional support to earlier findings.

Social Cognition

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Behere et al., 2011	0.392	0.266	0.071	-0.131	0.914	1.470	0.142
Jayaram et al., 2013	0.754	0.396	0.157	-0.022	1.531	1.904	0.057
	0.505	0.221	0.049	0.071	0.938	2.262	0.022

Statistics for each study

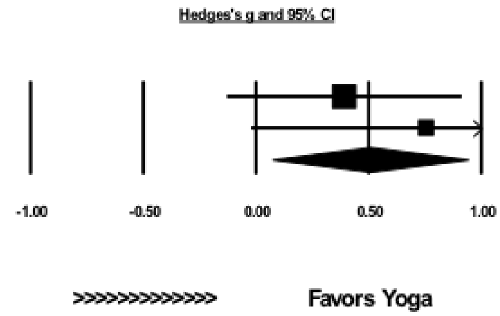

Figure 5. Overall Effect of Yoga on Social Cognition

Memory

Of the six studies included in the quantitative synthesis, three studies involving 90 participants assessed the effects of yoga on memory (Eyre et al., 2016; Eyre et al., 2017; Lin et al., 2015). A significant modest effect was found, g = .510 (SE = .157, 95% CI = .202 - .819, p = 0.01, I^2 = 0%, the random-effects model; Figure 6). Other studies have similarly examined the effects of yoga on cognition in neuropsychiatric populations, but have failed to report sufficient data from which to compute an effect (Bhatia et al., 2016; Oken et al., 2004). Lending further support for the positive effects of yoga on memory, Bhatia and colleagues (2016) reported yoga-related improvements on several domains of memory in schizophrenia as measured by the Penn CNB. For the speed index of the Penn CNB, results indicated that the yoga intervention group performed significantly better than the treatment as usual control group on spatial memory and face memory (Bhatia et al., 2016). Oken et al. (2004), however, found no statistically significant effects of yoga on memory in patients with multiple sclerosis as measured by the Wechsler Memory Scales III Logical Memory (delayed memory adjusted for immediate recall). The conflicting results were not factored into the pooled analyses, thereby potentially confounding sub-analysis results computed for the cognitive domain of memory.

Memory

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Lin et al., 2015	0.631	0.279	0.078	0.084	1.178	2.261	0.024
Eyre et al., 2017	0.445	0.232	0.054	-0.010	0.901	1.916	0.055
Eyre et al., 2016	0.472	0.332	0.110	-0.179	1.123	1.421	0.155
	0.510	0.157	0.025	0.202	0.819	3.244	0.001

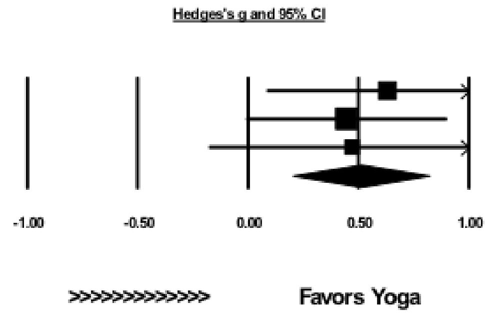

Figure 6. Overall Effect of Yoga on Memory

Attention and Processing Speed

Of the six studies included in the quantitative synthesis, two studies involving 53 participants assessed the effects of yoga on attention and processing speed in neuropsychiatric populations (Lin et al., 2015; Sharma et al., 2006) as measured by the Letter Cancellation Test (Uttl & Pilkenton-Taylor, 2001). A significant modest effect was found, g = .439 (SE = .20, 95% CI = .047 - .831, p = .028, I^2 = 0%, the random-effects model; Figure 7). Four other RCTs included in the qualitative synthesis examined the effects of yoga on attention in neuropsychiatric populations (Bhatia et al., 2016; Jensen & Kelly, 2004; Oken et al., 2004; Velikonja et al., 2010). Lending further support to the meta-analytic findings, Bhatia et al. (2016) found yoga-related improvements on attention as measured by the speed index of the Penn CNB. Further, Velikonja et al. (2010) reported significant yoga-related improvements on attention as measured by the d2 test of attention (Bates & Lemay, 2004). In contrast, Jensen and Kelly (2004) did not find significant yoga-related improvements on attention as measured by the TOVA (Braverman et al., 2010). Oken et al. (2004), administering a battery of tests to examine attention, also found no significant yoga-related improvements on attention. Unfortunately, insufficient data was available from these four studies to compute an effect size. In summary, meta-analytic findings as well as studies included in the qualitative synthesis offer moderate support for yoga's utility as an intervention to improve attention; however, these results are not without conflict. The conflicting results were not factored into the pooled analyses, thereby potentially confounding sub-analysis results computed for the cognitive domain of attention.

Attention and Processing Speed

Study name	Statistics for each study						
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Lin at al., 2015	0.473	0.241	0.058	-0.000	0.946	1.958	0.050
Sharma et al., 2006	0.365	0.358	0.128	-0.337	1.066	1.019	0.308
	0.439	0.200	0.040	0.047	0.831	2.193	0.028

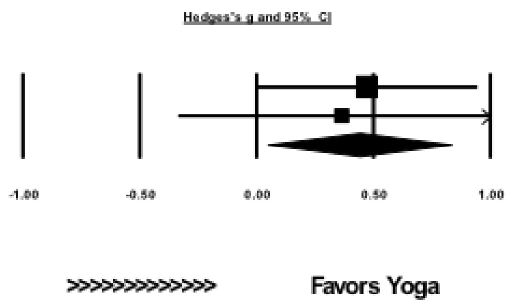

Figure 7. Overall Effect of Yoga on Attention and Processing Speed

Executive Function

Of the studies included in the quantitative synthesis, three studies involving 91 participants assessed the effects of yoga on executive function in neuropsychiatric populations (Eyre et al., 2017; Lin et al., 2015; Sharma et al., 2006). A significant modest effect was found, g = .448 (SE = .156, 95% CI = .143 - .754, p = .004, I^2 = 0%, the random-effects model; Figure 8). Two other studies included in the qualitative synthesis examined the effects of yoga on executive functioning using a battery of neuropsychological tests (Oken et al., 2004; Velikonja et al., 2010). Both studies, lacking sufficient data from which to compute an effect, indicated no significant yoga-related improvements on tests evaluating executive function. In summary, while meta-analytic findings support yoga's utility as an intervention to improve executive functioning in neuropsychiatric populations, other lines of evidence indicate a non-significant effect. These conflicting results were not factored into the pooled analyses, thereby potentially confounding sub-analysis results computed for the cognitive domain of executive function.

Executive Function

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Eyre et al., 2017	0.414	0.234	0.055	-0.044	0.872	1.773	0.076
Lin et al., 2015	0.479	0.257	0.066	-0.024	0.982	1.866	0.062
Sharma et al., 2006	0.469	0.363	0.132	-0.242	1.179	1.292	0.196
	0.448	0.156	0.024	0.143	0.754	2.873	0.004

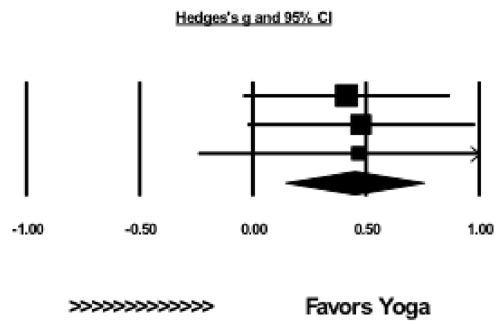

Figure 8. Overall Effect of Yoga on Executive Function

Schizophrenia Spectrum Disorders

Of the studies included in the quantitative synthesis, three studies involving 80 participants examined the effects of adjunctive yoga therapy on cognitive function in schizophrenia spectrum disorders. Overall, a significant modest effect was found, *g* = .515 (SE = .123, 95% CI = .273 - .757, *p* = .000, I^2 = 0%, the random-effects model; Figure 9). A pooled effect was computed for each of the four cognitive domains. Results indicated a significant modest effect on attention *g* = .473 (SE = .241, 95% CI = -.000 - .946, *p* = .050); a non-significant effect for executive functioning (*p* = .062); a significant modest effect on memory, *g* = .631 (SE = .279, 95% CI = .084 - 1.178, *p* = .024); and a significant modest effect for social cognition as previously reported, *g* = .505 (SE = .221, 95% CI = .071-.938, *p* = .022, I^2 = 0%, the random-effects model; Figure 5). Bhatia et al.

(2016) lend further support to these findings. For the speed index of the Penn CNB, the authors reported significant yoga-related improvements for memory (i.e., spatial memory and facial memory), attention, and social cognition (i.e., emotion processing). For the accuracy index, significant yoga-related improvements were found for abstraction and mental flexibility (Bhatia et al., 2016), a finding slightly at odds with the meta-analytic findings indicating a non-significant effect of yoga on executive functioning. In summary, studies included in the quantitative and qualitative syntheses provide moderate support for yoga's cognition-enhancing utility in schizophrenia spectrum disorders; however, findings suggest that these effects may not extend to the cognitive domain of executive function.

Schizophrenia

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Lin et al., 2015	0.520	0.149	0.022	0.228	0.812	3.494	0.000
Behere et al., 2011	0.392	0.266	0.071	-0.131	0.914	1.470	0.142
Jayaram et al., 2013	0.754	0.396	0.157	-0.022	1.531	1.904	0.057
	0.515	0.123	0.015	0.273	0.757	4.173	0.000

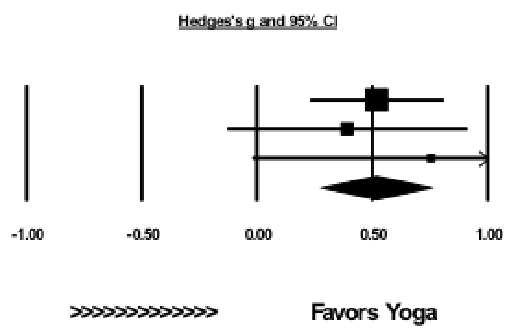

Figure 9. Overall Effect of Yoga on Cognitive Function in Schizophrenia

Mild Cognitive Impairment

Of the six studies included in the quantitative synthesis, two studies involving 52 participants examined the effects of adjunctive yoga on cognitive function in patients with mild cognitive impairment (Eyre et al., 2016; Eyre et al., 2017). Overall, a significant modest effect was found, g = .438 (SE = .148, 95% CI = .149 - .728, p = .003, I^2 = 0%, the random-effects model; Figure 10). Results further indicated a non-significant effect for executive function (p = .076) and a significant modest effect on memory, g =

.454 (SE = .190, 95% CI = .081-.827, p = .017, I^2 = 0%, the random-effects model; Figure 11). Attention tests were not administered. In summary, studies provide moderate support for yoga's cognition-enhancing utility for mild cognitive impairment; however, findings suggest that these positive effects may not extend to the cognitive domain of executive function.

MCI (Overall Effect)

Study name	Statistics for each study						
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Eyre et al., 2016	0.472	0.332	0.110	-0.179	1.123	1.421	0.155
Eyre et al., 2017	0.430	0.165	0.027	0.107	0.753	2.609	0.009
	0.438	0.148	0.022	0.149	0.728	2.968	0.003

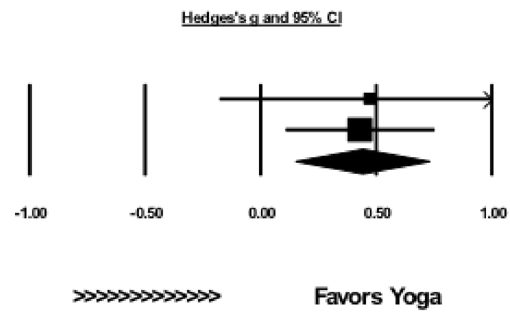

Figure 10. Overall Effect of Yoga on Cognitive Function in Mild Cognitive Impairment

MCI (Memory)

Study name	Statistics for each study						
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Eyre et al., 2016	0.472	0.332	0.110	-0.179	1.123	1.421	0.155
Eyre et al., 2017	0.445	0.232	0.054	-0.010	0.901	1.916	0.055
	0.454	0.190	0.036	0.081	0.827	2.384	0.017

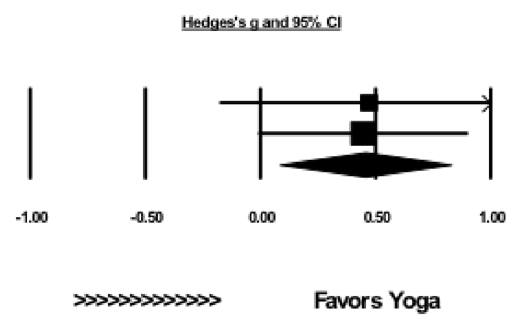

Figure 11. Overall Effect of Yoga on Memory in Mild Cognitive Impairment

Attention-Deficit/Hyperactivity Disorder

One study, included in the qualitative synthesis, examined the effects of yoga on attention in subjects with attention-deficit/hyperactivity disorder as measured by the Test of Variables of Attention (TOVA) (Jensen & Kelly, 2004). No significant yoga-related effects were found. Data was unavailable from which to compute an effect; therefore, these findings were not factored into the pooled analyses. In summary, results indicate no support for yoga's attention-enhancing utility for attention-deficit/hyperactivity disorder, a finding that should be interpreted cautiously as it arises from one study with a small sample size.

Multiple Sclerosis

Two studies, included in the qualitative synthesis, assessed the effects of yoga on cognition function in multiple sclerosis (Oken et al., 2004; Velikonja et al., 2010). Oken et al. (2004) administered a battery of cognitive tests focused on aspects of attention (focusing attention, shifting attention, dividing attention, and sustaining attention), executive functioning, and memory. No significant yoga-related improvements were found on any of the cognitive outcome measures (Oken et al., 2004). Similarly, Velikonja et al. (2010) administered a battery of tests assessing executive functioning and attention. Similar to Oken and colleagues (2004), no significant improvements were found on tests of executive functioning; however, the authors reported a significant effect of yoga on attention. Both studies provided insufficient data from which to compute an effect; therefore, these findings were not factored into the pooled analyses. Results from these two studies suggest that yoga has limited cognition-enhancing utility for multiple sclerosis, specifically in cognitive domains of executive functioning and memory. While evidence is limited, yoga might, however, provide some benefit in the cognitive domain of attention and processing speed for multiple sclerosis.

Major Depressive Disorder

One study examined the effects of adjunctive yoga on neurocognitive function in adult subjects with major depressive disorder (Sharma et al., 2006). Results indicated no significant overall effect (p = .103). Further, subgroup analyses showed no significant effect when the pooled effect size was computed for attention (p = .308) and executive functioning (p = .196). Tests assessing memory were not administered. The non-significant pooled effect results were surprising given the authors' findings that adjunctive yoga (i.e., yoga and antidepressants) lead to significant added improvement in attention span, concentration, and visuo-motor speed as well as improvement in the executive functioning of verbal working memory, auditory attention, and short-term retentive capacity as compared to antidepressants-only (Sharma et al., 2006). While significant yoga-related improvements were evidenced on individual tests assessing attention and executive functioning (e.g., the time for the Letter Cancellation Test evidenced significant yoga-related improvement), the pooled effect analysis (i.e., all of the tests assessing attention) yielded contradictory results, perhaps owing to the small sample size. Importantly, there was insufficient data reporting for several neuropsychological tests administered in Sharma et al.'s (2006) study. The authors reported no significant yoga-related changes on the RFFT, forward digit span test, and commissions on the Letter Cancellation Test, but data was incomplete (e.g., missing p-values), preventing an effect size computation (Sharma et al., 2006). Therefore, these non-significant findings for the cognitive domains of attention and executive functioning were not factored into the pooled analyses, thereby confounding the overall effect size computed for cognition and sub-analyses computed for cognitive domains of attention and processing speed and executive function. To summarize, results suggest that yoga confers no cognitive advantage for major depressive disorder; however, these findings should be cautiously interpreted as they arise from one study with a small sample size.

Effects on Mood

Of the studies included in the quantitative synthesis, four studies involving 105 participants assessed depressive symptoms in neuropsychiatric populations (Eyre et al., 2016; Eyre et al., 2017; Lin et al., 2015; Sharma et al., 2006). A large significant overall effect was found, g = .797 (SE = .274, 95% CI = .261 - 1.33, p = .004, I^2 = 63.73%, the random-effects model; Figure 12). Two other studies, included in the qualitative synthesis, assessed depressive symptoms in response to yoga (Oken et al., 2004; Velikonja et al., 2010). In contrast to meta-analytic findings, Oken et al. (2004) observed no significant overall improvements in the POMS subscales of depression or the CES-D in response to the yoga intervention employed. Similarly, Velikonja et al.'s (2010) evaluation of mood did not demonstrate any significant yoga-related improvement on depressive symptoms using the CES-D. Given these findings, the meta-analytic results, suggestive of yoga's robust utility as an intervention to improve depressive symptoms in neuropsychiatric populations, must be interpreted cautiously. Additionally, substantial heterogeneity was found (I^2 = 63.73%) further warranting cautious interpretation.

Depression

Studyname	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Lin et al., 2015	0.550	0.194	0.038	0.170	0.931	2.835	0.005
Eyre et al., 2017	0.477	0.237	0.056	0.012	0.942	2.010	0.044
Sharma et al., 2006	2.829	0.807	0.651	1.248	4.410	3.507	0.000
Eyre et al., 2016	0.843	0.419	0.176	0.022	1.664	2.012	0.044
	0.797	0.274	0.075	0.261	1.333	2.914	0.004

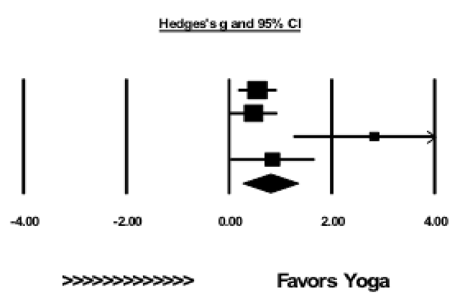

Figure 12. Overall Effect of Yoga on Depression

Adverse Effects

Adverse effects were minimal in response to the yoga interventions. Only one study reported that a participant withdrew from the yoga intervention due to dizziness (Eyre et al., 2017). In addition, two participants reported exacerbation of symptoms and withdrew from the yoga intervention; however, the authors explicitly reported that no adverse effects occurred in response to the yoga intervention (Bhatia et al., 2016). Therefore, worsening of symptoms may not have been attributable to the yoga intervention, but rather, arose spontaneously or in response to extraneous variables (Bhatia et al., 2016). Five studies reported no adverse effects in response to the yoga intervention (Bhatia et al., 2016; Lin et al., 2015; Oken et al., 2004; Sharma et al., 2006); however, five studies did not address adverse effects (Behere et al., 2011; Eyre et al., 2016; Jayaram et al., 2013; Jensen & Kelly, 2004; Velikonja et al., 2010). Overall, the available evidence suggests that yoga is a relatively safe intervention to employ in neuropsychiatric populations; however, several studies did not report on safety data, thereby limiting any definitive conclusion.

Barriers to Adherence

Several studies reported on barriers to yoga intervention adherence. Behere et al. (2011) reported that patients dropped out because they were not adherent to the home practice structure. Though their compliance rates were satisfactory, Bhatia et al. (2016) reported several barriers to adherence including transportation difficulties, location (i.e., too far), practice hour (i.e., too early), symptom aggravation unrelated to the yoga intervention, and home practice adherence. Lin et al.'s (2015) dropout analyses showed that non-adherent patients had larger deficits in cognition and were more severely ill.

Eyre et al. (2016) reported dropouts due to lack of interest in the intervention or inability to commit to the practice schedule. Similarly, Jayaram et al. (2013) reported that logistical conflicts were the main barriers to treatment adherence. Finally, Oken et al. (2004) reported that other family health issues, time constraints, location (i.e., too far), personal health issues, and symptom exacerbation impeded yoga intervention adherence. Other studies did not offer information regarding yoga intervention adherence factors (Eyre et al., 2017; Jensen & Kelly, 2004; Sharma et al., 2006; Velikonja et al., 2010). Taken together, studies suggest that home practice, location, and symptom aggravation might complicate adherence. Also, individuals with more severe cognitive function or symptoms may be less likely to benefit from yoga (Lin et al., 2015).

CHAPTER 5

DISCUSSION

Summary

This systematic review and meta-analysis evidences some preliminary, yet provisional support for yoga as an adjunctive therapy to improve domains of cognition in patient populations with a broad landscape of neuropsychiatric disorders. Although only six studies were included in the quantitative synthesis, findings provide encouraging effects of yoga for patients with neuropsychiatric disorders on important clinical outcomes, including improvements in several domains of cognitive performance. Regarding global cognitive function, the pooled overall effect suggests that yoga confers moderate improvements in cognition in patients with a range of neuropsychiatric disorders including schizophrenia spectrum disorders and mild cognitive impairment. Within the specific domain of social cognition, yoga showed a moderate effect, specifically in patients with schizophrenia. For the neuropsychological domains of attention and processing speed, memory, and executive function, sub-analyses further evidenced moderate support for yoga's utility across several neuropsychiatric disorders, with the strongest effect for memory, followed by executive function, and attention and processing speed.

In evaluating neuropsychiatric subgroups, the most robust evidence supported yoga's cognition-enhancing utility for schizophrenia spectrum disorders. Meta-analytic results indicated a moderate overall effect on cognition, with the strongest effect for memory, followed by social cognition, and attention and processing speed; a non-significant effect was found for executive function. For mild cognitive impairment, an overall moderate effect was found on cognition with the strongest effect on memory; a non-significant effect was found for executive function and no conclusions could be made regarding attention and processing speed as these tests were not administered within this subgroup. For attention-deficit/hyperactivity disorder, there was no evidence supporting yoga's cognition-enhancing utility. This aligns with earlier findings (Lange et al., 2014). Similarly, for major depressive disorder, there was lack of evidence supporting yoga's cognition-enhancing utility. For multiple sclerosis, the qualitative synthesis indicated that, overall, yoga conferred little cognitive advantage; however, there was some evidence to suggest that yoga contributed to improvements in the domain of attention and processing speed. Interestingly, meta-analytic results did not evidence any improvements in executive functioning regardless of diagnosis, suggesting that yoga might be more efficacious in domains of memory, attention and processing speed, and social cognition.

On secondary outcomes, meta-analytic results showed a strong effect of yoga on depressive symptoms. Perhaps yoga-related improvements in cognitive deficits are mediated by reduction in depressive symptomology, a relationship that has previously been discussed (Mathersul & Rosenbaum, 2016) and one that future yoga studies should investigate. Importantly, of the included studies, only one adverse event related to yoga was reported in the patient sample. This confirms the general consensus that yoga is a relatively safe intervention (Anand & Verma, 2014; Balasubramaniam et al., 2013; Field, 2017; Mooventhan & Nivethitha, 2017; Rao et al., 2013); however, several studies included in this review did not report on safety outcomes. This omission of safety data, a previously discussed oversight (Anand & Verma, 2014), is one that future studies can easily amend. In the review of barriers to adherence, Lin et al. (2015) evidenced a positive correlation between non-completers of the yoga intervention and more severe scores on cognitive measures. The tolerability, then, to adhere to a yoga intervention may not be comparable across all individuals and may very well depend on the extent of the cognitive impairment and other symptoms. Other barriers included difficulty with home practice adherence, location, and symptom exacerbation; nevertheless, adherence to yoga interventions was satisfactory across studies. Indeed, patients and caregivers often provided positive feedback regarding intervention outcomes. Several patients expressed satisfaction with yoga (Eyre et al., 2017), some reporting that the practice made them more active (Bhatia et al., 2016). Caregivers repeatedly inquired about new yoga therapy programs after completion of the intervention, suggesting their satisfaction with the outcome (Bhatia et al., 2016). Additional anecdotal evidence from parents and participants suggested improvements in the behavior of boys with attention-deficit/hyperactivity disorder in response to yoga, including increased behavioral regulation, decreased restlessness, improved sleep, improved memory, and increased ability to cope with multiple instructions (Jensen & Kelly, 2004). Further, in patients with multiple sclerosis, trainers subjectively observed an increase in patients' motivation, enthusiasm, and interest in socializing with each other in response to yoga (Velikonja et al., 2010). This supports earlier evidence suggesting that yoga is generally well-received (Balasubramaniam et al., 2013).

Taken together, this review evidences positive yoga-related effects on cognition and depressive symptoms with low risk of side effects in neuropsychiatric populations. At this point, these effects should be interpreted optimistically, but with caution.

Limitations

While the meta-analytic results favor adjunctive yoga therapy for improving cognition across several neuropsychiatric disorders, the studies reviewed are ripe with methodological limitations including small sample sizes, inadequate control conditions, diverse yoga protocols, wide-ranging cognitive outcome measures, lack of safety data, publication bias, selective data reporting, and varied assessment time points.

First, yoga protocols considerably varied across the 10 reviewed studies in terms of style, structure, frequency, and duration of practice sessions (see Appendix D). This variability might detract from determining the optimal content (e.g., asana, breath regulation techniques, meditation, etc.) of yoga for cognitive improvement in neuropsychiatric disorders. Optimizing and standardizing these protocols might encourage increased adherence, better patient outcomes, and increased generalizability and replicability of findings. Few studies, however, have attempted to standardize yoga protocols. Only one study, for example, has attempted to validate a yoga protocol for schizophrenia (Govindaraj, Varambally, Sharma, & Gangadhar, 2016). In their study, Govindaraj and colleagues (2016) aimed to develop a generic yoga-based intervention protocol for patients with schizophrenia, recruiting 10 yoga experts to validate items on the protocol and recommend modifications. Experts concluded that conscious breathing exercises and loosening exercises were important and should be retained in the module and agreed with the duration of one-hour daily training for one month under supervision as adequate for subsequent practice at home, which aligns with some of the protocols of the studies reviewed (Govindaraj et al., 2016). More expert-validated studies such as these should be considered in the future to better inform safe and accessible yoga protocols. It must be noted, however, that while there are clear benefits to standardizing yoga protocols for research, it is important to adapt yoga therapies to the individual (Bhatia et al., 2016). For example, content may need to be adjusted while working with patients more prone to balance disturbances. Physiotherapists and yoga therapists should assess what types of movement practices align with patient needs and preferences and should frequently monitor their responses and progress (Vancampfort et al., 2011). While this creates difficulties for implementing standardized RCT protocols in research, it might promote continued adherence to a clinical exercise program. In other words, if patients feel competent in practice, they might be more likely to continue with the program.

Similarly, the outcome measures related to cognitive function in the included studies were wide-ranging (see Appendix E). Most of the measurement methods, such as Stroop Color and Word Test and the Letter Cancellation Test (Uttl & Pilkenton-Taylor, 2001), were objective and had high validity and reliability. Of the 10 studies included, however, none provided a measure of global cognitive function, such as the Mini-Mental State Examination (MMSE) (Kulas & Naugle, 2003). Future studies should make use of more objective testing methods or instruments for global cognition so that effect sizes can be calculated. It is possible that the variety of non-compatible measurement tools used confounds the computation of the pooled overall effect on cognition. Future studies might also make use of more objective testing methods or instruments (e.g., event-related potential and functional MRI). The effect of yoga on different cognitive domains was also evaluated in all included studies, but few studies measured the same cognitive domain using the same measurement tools. Furthermore, most cognitive domains included small numbers of studies and samples. Thus, the measurement methods and data heterogeneity may confound the positive effects computed. While heterogeneity appeared low, the I^2 statistic has a substantial bias when the number of studies is small and, therefore, should be interpreted cautiously (Von Hippel, 2015).

In addition, several types of potential bias must be addressed. It is impossible to blind participants in a yoga intervention trial; therefore, performance bias may be inevitable. Additionally, several studies did not specify the blinding parameters of assessors; therefore, observer bias might also have been high; however, these studies used objective measures to assess improvement thus limiting the potential for observer bias. However, future studies should employ more rigorous blinding parameters and explicitly state the way in which blinding was achieved throughout the study. While publication bias was not observed by funnel plot analysis, this is likely due to the insufficient number of included studies. The included studies were also limited by the small participant numbers, which most likely inflated type I error and contributed to low statistical power. Further, selective reporting or insufficient data reporting was judged as unclear and/or high owing to missing data from which to compute an effect size in several studies. In future studies, whether findings prove significant or not, authors should report statistics from which an effect size can be computed so that evidence-based reviews such as these can pool effect sizes that are more representative of findings. In summary, the overall strength of the evidence in this review should be interpreted with caution.

Clinical Implications and Recommendations for Future Studies

In patients with a broad landscape of neuropsychiatric disorders, yoga appears to improve overall cognitive function, especially in the cognitive domains of attention and processing speed, memory, and social cognition. Yoga also produced markedly limited adverse effects, suggesting that it might be a feasible intervention for patients with neuropsychiatric disorders. This provides clinicians with cautiously optimistic evidence of an effective, relatively safe adjunctive therapy to recommend to patients with cognitive decline. The evidence for schizophrenia spectrum disorders is most robust, especially for social cognition, memory, and attention and processing speed, and for mild cognitive impairment, for memory.

Future studies in this field should evaluate the appropriate training intensity, sequence, duration, and frequency of yoga training protocols through expert-validated protocols (Govindaraj et al., 2016) and might also benefit from implementing more standardized, yet modifiable practice styles, such as Iyengar Yoga, an alignment-based practice (Woodyard, 2011). Iyengar Yoga, with its higher prerequisite standards and more extensive teacher training and certification process, is a practice with established quality, accessibility, and safety (Iyengar Yoga: National Association of the United States, n.d.). Therefore, it is proposed that future interventions borrow from the Iyengar Yoga method (or other methods that arose from it, such as Eischens Yoga), ideally appointing certified Iyengar instructors to both design and carry out yoga interventions. Further, if possible, studies should perform assessments at various time points to determine the temporal pattern by which improvements are gained and ultimately, maintained. Global cognitive ability as well as specific domains of cognition such as memory, attention, executive function, and social cognition should be assessed, and more sensitive and objective measurement tools should be used. In addition, authors should adhere to CONSORT guidelines when reporting their studies to allow better evaluation of methodological quality (Cramer et al., 2015) and should also provide complete statistical data. Further, there is a need for larger, more heterogeneous cohort studies as all studies reviewed were single-site (Lin et al., 2015). Future yoga studies should deal with patient samples from multiple institutions and cultural ethnic backgrounds to improve generalizability and recommendations for practice. For example, an Iyengar Yoga protocol might be tested at various clinical sites to determine its global effectiveness for patients with neuropsychiatric disorders, and also, to better detect potential contraindications that necessitate protocol modification.

Conclusion

There is considerable hype surrounding yoga practice (Balasubramaniam et al., 2013), which, in part, motivated this evidence-based review. Yoga is often perceived and prescribed as a sort of cure-all, which, as this review and others evince, is a misguided, inflated conclusion. Yoga, like any other system, has its limitations and challenges (Patwardhan, 2016); however, preliminary evidence does show some promising utility for the practice and this should encourage future study into the potential of yoga interventions for cognitive health in neuropsychiatric populations. Running counter to the yoga messages often marketed to the public, the genuine article of yoga practice is unity (Iyengar, 1965). In the yoga philosophy, a disconnect from the self is thought to be source of suffering (Iyengar, 1965). Yoga, then, provides the practitioner with a potent way of bypassing the conscious, defensive, reactive, and egoic mind, in order to facilitate that reconnection with the mind and body, a connection that modern society is paying more attention to, but still largely dismisses as being critical to health and wellness (Mehta, 2011). The dichotomization of mind and body is still pervasively practiced in society, especially in clinical milieus and medical disciplines (e.g., major depressive disorder is a mental disorder whereas multiple sclerosis is a more physical brain disorder despite sharing significant comorbidity and symptom overlap) (Mehta, 2011). Yoga challenges this mind-body duality with its emphasis on unity, the essence of practice. Yoga, at least in its traditional form, is not simply a physical modality (Iyengar, 1965). When practiced in its intended way, yoga is a body-based system with an intentional, meditational component (Iyengar, 1965). The intentional, meditational component is what differentiates yoga from most other movement practices, and therefore, it is proposed that this component receive more study. Mindfulness scales, for example, might be administered to determine if improvements in mindfulness correlate with improvements in the regulation of attention and/or affect (e.g., depression) and mediate other cognitive outcomes. The mindful, intentional component should be parsed out and evaluated more closely so that more empirically founded mechanisms can be tested for the way by which yoga confers cognitive advantage in patients with neuropsychiatric disorders.

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APPENDIX A

PRISMA 27-ITEM CHECKLIST

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	i
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	iii
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	47
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	47
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	50

Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	95
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	50
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	51
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	50
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	50
Summary measures	13	State the principle summary measures (e.g., risk ratio, difference in means).	51
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	51

Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	50
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	50
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	53
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	54

Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	55
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	58
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	58
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	55
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	58
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	71
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	74
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	78
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

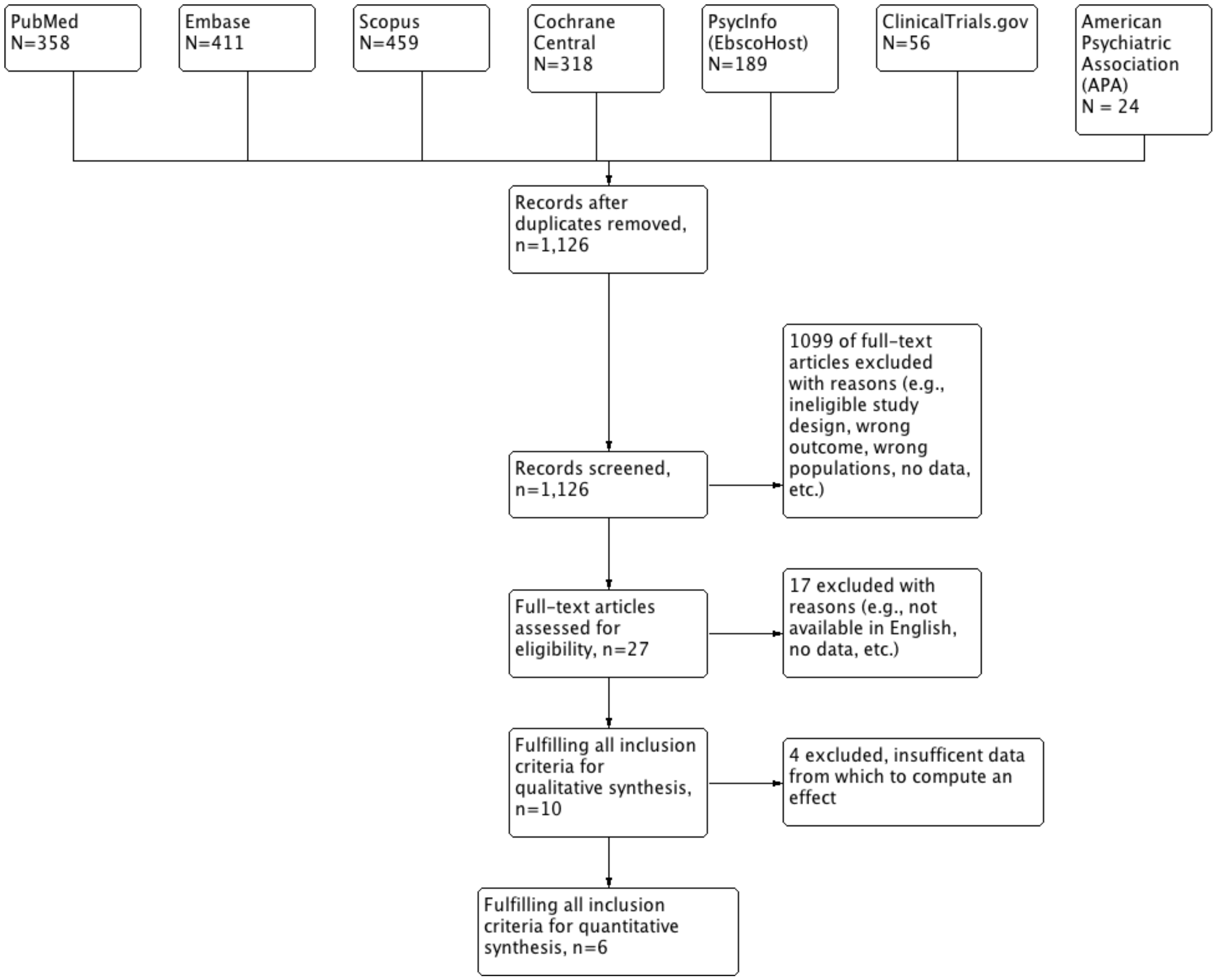
APPENDIX B

SEARCH STRATEGY FOR PUBMED (NLM)

#1
(Cognition[tw] OR cognitive[tw] OR "social cognition"[tw] OR "cognitive deficit"[tw] OR "cognitive deficits"[tw] OR "cognitive dysfunction"[tiab] OR "cognitive dysfunctions"[tiab] OR "cognitive impairment"[tw] OR "cognitive impairments"[tw] OR FERD[tw] OR FERDs[tw] OR "facial emotion recognition deficits"[tw] OR "facial emotion recognition deficit"[tw] OR schizophrenia[tiab] OR "early psychoses"[tw] OR psychoses[tw] OR "psychotic disorder"[tw] OR "neurocognitive disorder"[tiab] OR "neurocognitive disorders"[tiab] OR "neurocognitive disorder"[tiab] OR "neurocognitive disorders"[tiab] OR "neurocognitive function"[tw] OR "neurocognitive functions"[tw] OR "neuro cognitive function" OR "neuro cognitive functions"[tw] OR "memory disorders"[tw] OR "memory disorder"[tw] OR dementia[tw] OR "brain trauma"[tw] OR "cognitive domain"[tw] OR "cognitive domains"[tw] OR "affective disorder"[tw] OR "affective disorders"[tw] OR "mood disorder"[tw] OR "mood disorders"[tw] OR ADHD[tw] OR "attention deficit disorder"[tw] OR "attention deficit disorders"[tw] OR "hyperactivity disorder"[tw] OR "hyperactivity disorders"[tw] OR "attention deficit hyperactivity disorder"[tw] OR "attention deficit hyperactivity disorders"[tw] OR "Cognition"[Mesh] OR "Cognition Disorders"[Mesh] OR "Emotion-Focused Therapy"[Mesh] OR "Expressed Emotion"[Mesh] OR "Psychotherapy"[Mesh] OR psychotherapy[tiab] OR "Schizotypal Personality Disorder"[Mesh] OR "Schizophrenia, Paranoid"[Mesh] OR "Schizophrenia Spectrum and Other Psychotic Disorders"[Mesh] OR "Schizophrenia"[Mesh] OR "Schizophrenia, Disorganized"[Mesh] OR "Schizophrenia, Childhood"[Mesh] OR "Schizophrenia, Catatonic"[Mesh] OR "Neurocognitive Disorders"[Mesh] OR "Cognitive Dysfunction"[Mesh] OR "Dementia"[Mesh] OR "Frontotemporal Dementia"[Mesh] OR "Affective Disorders, Psychotic"[Mesh] OR "traumatic psychoses"[tw] OR "Attention Deficit Disorder with Hyperactivity"[Mesh] OR ADDH[tiab] OR "minimal brain dysfunction"[tw] OR "minimal brain dysfunctions"[tw] OR "affective psychoses"[tw] OR "psychotic affective disorder"[tw] OR "psychotic affective disorders"[tw] OR "psychotic mood disorder"[tw] OR "psychotic mood disorders"[tw] OR "psychotic reactive depression"[tw] OR "Affective Symptoms"[Mesh] OR "affective symptom"[tiab] OR "affective symptoms"[tiab] OR alexithymia[tiab] OR alexithymias[tiab])
884,596 results
#2
(yoga[tiab] OR yogic[tw] OR "Yoga"[Mesh])
3,991 results
#3
(yoga[tw] AND "facial emotion recognition deficits"[tw])
2 results
#4
#2 OR #3
3,991 results
#5
#1 AND #4
1,123 results
#6
#5 AND (random*[Title/Abstract])
358 results

APPENDIX C

STUDY FLOW DIAGRAM



APPENDIX D

CHARACTERISTICS OF INCLUDED STUDIES

Author, year	**Disorder**	**Mean Age**	**N (M:F)**	**Intervention**	**Assessments, frequency, time/session**	**Primary/secondary outcome measures**
Behere et al., 2011	Schizophrenia (DSM-IV)	31.7	66 (47:19)	T: SVYASA yoga therapy protocol AC: Exercise, brisk walking, jogging, etc. C: WL/TAU	Baseline, 2 months, 4 months 1hr/session	Social cognition/TRENDS
Bhatia et al., 2016	Schizophrenia (DSM-IV)	35.24	286 (181:105)	T: Yoga therapy/TAU AC: Exercise/TAU C: TAU	Baseline, 21 days, 3 months, 6 months 1hr/session	Accuracy and speed indices for abstraction and mental flexibility for attention; face memory; spatial memory; spatial processing; working memory; sensorimotor dexterity; emotion processing/ Penn CNB
Eyre et al,. 2016	Mild Cognitive Impairment	67.45	25 (13:12)	T: Kundalini yoga (KY) and Kirtan Kriya (KK) AC: Memory Enhancement Training	Baseline, 12 weeks 60 mins KK/week 12 mins KK/day	Verbal learning and memory/HVLT-R; Visuospatial memory/RCFT Depression/GDS
Eyre et al., 2017	Mild Cognitive Impairment	67.85	79 (27:52)	T: Kundalini yoga and Kirtan Kriya AC: Memory Enhancement Training	Baseline, 12 weeks, 24 weeks 60 mins KK/week 12 mins KK/day	Verbal learning and memory/HVLT; Global memory/WMS-IV; Visuospatial memory/RCFT; Attention/TTA; Executive function/TTB; Stroop test; ANT Depression/GDS
Jayaram et al., 2013	Schizophrenia (DSM-IV)	28.92	27 (19:8)	T: SVYASA yoga therapy protocol C: Waitlist	Baseline, 1 month 60mins/session	Social cognition/TRENDS
Jensen et al., 2004	Attention-Deficit/ Hyperactivity Disorder (DSM-IV)	9.9	14 (14:0)	T: Yoga AC: Cooperative games	Baseline, 20 sessions 1 session/week	Attention/TOVA
Lin et al., 2015	Schizophrenia Spectrum Disorders (DSM-IV)	24.57	124 (0:124)	T: Integrated yoga therapy AC: Aerobic exercise C: Waitlist	Baseline, 12 weeks, 18 months 3 times/week, 60mins/session	Verbal memory/HKLLT; Memory/digit span forwards; Attention/LCT; Executive function/Stroop test; digit span backwards Depression/CDS

Oken et al., 2004	Multiple sclerosis	49	57 (4:53)	T: Iyengar Yoga AC: Cycling and stretches C: Waitlist	Baseline, 6 months 1/week, 60mins/session	Executive function /Stroop test; attentional shifting task; Useful Field of View task; WAIS-III Similarities Attention/PASAT; Memory/WMS-III Depression/POMS; CES-D
Sharma et al., 2006	Major depressive disorder	31.77	30 (19:11)	T: Sahaj Yoga meditation and conventional anti-depressant medication C: Conventional anti-depressant medication	Baseline, 8 weeks 3 times/week, 30mins/session	Attention/LCT; TTA Executive function/TTB; RFFT; digit span backwards Memory/digit span forwards Depression/HAM-D
Velikonja et al., 2010	Multiple sclerosis	NR	20 (NR:NR)	T: Hatha yoga AC: Sport climbing	Baseline, 10 weeks 1 session/week	Executive function/Mazes subtest; TOL; Attention/d2 Depression/CES-D

APPENDIX E

CLASSIFICATION OF THE NEUROPSYCHOLOGICAL TESTS BY COGNITIVE DOMAIN AND DEPRESSION SCALES

Primary Outcomes				Secondary Outcomes
Attention and Processing Speed	Executive Function	Memory	Social Cognition	Depression
Trail Making Test, Part A, TTA (2) Letter Cancellation Test, LCT (2) Brickenkamp d2 Test (1) Test of Variables of Attention, TOVA (1) Paced Auditory Serial Addition Test, PASAT (1)	Stroop Word and Color Test (3) Digit span, backwards (2) Trail making test, part B, TTB (2) Mazes subtest of Executive module from the Neuropsychological assessment battery, NAB (1) Attentional shifting task (1) Useful field of view task (1) Wechsler Adult Intelligence Scale III Similarities, WAIS-III (1) Animal naming test, ANT (1) Tower of London test, TOL (1) Ruff figural fluency test, RFFT (1)	Hopkins Verbal Learning Test - Revised, HVLT-R (2) Rey-Osterrieth Complex Figure Task, RCFT (2) Digit span, forwards (2) Hong Kong List Learning test, HKLLT (1) WMS-III Logical Memory (1) WMS-IV (1)	Tool for Recognition of Emotions in Neuropsychiatric Disorders, TRENDS (2) Emotion processing, University of Pennsylvania computerized neurocognitive battery, Penn CNB (1)	Geriatric Depression Scale, GSD (2) Calgary Depression Scale, CDS (2) Hamilton Depression Rating Scale, HAM-D (1) Profile of Mood States, POMS (1) Center for Epidemiologic Studies Depression Scale, CES-D (2)