

# War-Related Mental Health Issues and Need for Yoga Intervention Studies: A Scoping Review

## Abstract

Conflicts and humanitarian crises lead to serious mental health disorders, including depression, anxiety, stress, and cognitive decline. Exposure to these circumstances in early life can lead to the development of disorders such as mild cognitive impairment, dementia, and Alzheimer's disease (AD), for which no treatments are available. In this review, various research papers have been compiled to develop an understanding about mental health of population affected due to wars and conflicts and how stress and depression can accelerate the development of dementia and AD. Due to failure of drugs in the treatment of dementia and AD, yoga and mindfulness-based approach has been proposed for future investigations. Although studies have shown that yoga and mindfulness can be helpful in the management of stress, anxiety, depression, and posttraumatic stress disorder in the war-afflicted areas, limited mechanistic studies in yoga and mindfulness remain the chief cause precluding its clinical application in such warzones. The molecular studies in the field of yoga can be undertaken by targeting these warzones. This review provides a scientific evaluation of mind-body techniques as a justification for mental health rehabilitation in the war-afflicted zones in face of failed clinical trials for various drugs. This may help reduce the risk of developing dementia and AD in this susceptible population.

**Keywords:** Cognitive impairment, dementia, memory, stress, war-prone area, yoga

## Introduction

War and conflicts cause extensive morbidity and mortality among the civilian population and military personnel in the war-affected area.<sup>[1]</sup> Along with those killed in violent conflicts, those who have experienced and suffered through these deaths (for example, maternal and infant mortality) are adversely affected at mental level.<sup>[2]</sup> It has been studied that people of war-prone areas suffer from various disorders which include various disabling injuries and adverse effects on the mental health, and these may even impair the future generations. Posttraumatic stress disorder (PTSD) and depression are the most common mental disorders among children and adults of war-affected areas.<sup>[3,4]</sup> Effects of war and conflicts in early life can affect mental health and development of mental disorders, such as depression and anxiety. In adverse cases, it may lead to the development of dementia and Alzheimer's disease (AD).<sup>[5]</sup> The locals of war-prone areas and armed forces in the area of conflicts are continuously being affected

by such stressful conditions.<sup>[6]</sup> Studies have shown that 25%–75% of survivors of artificial disasters develop PTSD.<sup>[7]</sup> A UNICEF study estimated in 1990 that, for every child death in war, three or more children are physically and psychologically disabled which ultimately led to 14 million children who were physically or psychologically traumatized by war during the 1980–1990.<sup>[8]</sup>

A study concluded that 22.1% of conflict-affected people have propensity to develop disorders such as depression, anxiety, stress, bipolar disorder, or schizophrenia at any time of ongoing conflict. The conditions such as these can lead to the development of dementia and AD,<sup>[9]</sup> and currently, no reliable treatment options and drugs are available for dementia and AD. Due to lack of an effective treatment for these disorders, there is a need to understand potentially modifiable risk factors for these conditions.<sup>[10]</sup> As there is high prevalence of these disorders in armed forces and residents of conflict-ridden

**Akshay Anand<sup>1,2,3</sup>,  
Abdul Ghani<sup>4</sup>,  
Kanupriya Sharma<sup>1</sup>,  
Gurkeerat Kaur<sup>1</sup>,  
Radhika Khosla<sup>1</sup>,  
Chandra Devi<sup>1</sup>,  
Vivek Podder<sup>5</sup>,  
Madhava S.  
Sivapuram<sup>6</sup>,  
Kalyan Maity<sup>7</sup>,  
Harmandeep Kaur<sup>8</sup>**

<sup>1</sup>Department of Neurology, Neuroscience Research Lab, Postgraduate Institute of Medical Education and Research, <sup>2</sup>CCRYN Center for Mind Body Interventions through Yoga PGIMER, <sup>3</sup>Centre for Cognitive Sciences and Phenomenology, Panjab University, <sup>4</sup>Department of Histopathology, Postgraduate Institute of Medical Education and Research, <sup>5</sup>Department of Physical Education, Panjab University, Chandigarh, <sup>6</sup>Department of Internal Medicine, Kamineni Institute of Medical Sciences, Nalgonda, Telangana, <sup>7</sup>Department of Medicine, Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Vijayawada, Andhra Pradesh, <sup>8</sup>Division of Yoga and Life Sciences, Swami Vivekananda Yoga Anusandhana Samsthana, Bengaluru, Karnataka, India

### Address for correspondence:

Prof. Akshay Anand,  
Department of Neurology,  
Neuroscience Research Lab,  
Post Graduate Institute  
of Medical Education and  
Research, Chandigarh, India.  
E-mail: akshay1anand@  
rediffmail.com

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areas, there is a need to identify the individuals at high risk for the prevention of disease in the presymptomatic stage; this can also be considered as a matter of high priority not only for Defense Department but also for the Alzheimer's research community.

Rehabilitation and treatment of conflict-affected population is one of the major concerns for the war-affected population as it is at high risk of being affected at mental, social, psychological, and physical well-being due to their routine stressful environment. The guidelines for mental rehabilitation have been published by certain national and professional agencies, e.g. the US Institute of Medicine 34; the American Psychiatric Association; the UK National Institute of Clinical Excellence; the World Federation of Societies of Biological Psychiatry; the Australian National Center for PTSD; and the British Association for Psychopharmacology.<sup>[11-15]</sup> These guidelines point toward the need of preventive measures for the management of mental health disorders due to war-afflicted stress that empower an endeavor to confide any unanticipated trauma and consequent PTSD. Interventions such as psychotherapy, psychoeducation, yoga and mindfulness-based intervention, and certain psychopharmacological interventions have been considered as both preventive and promotive in the management of disorders associated with conflict and war-related conditions. Of all the preventive measures prescribed for health management in war and conflict-related conditions, yoga can be a major rehabilitative intervention. Several studies have found that yoga can help in relieving stress,<sup>[16]</sup> perceived stress and work-related stress,<sup>[17]</sup> anxiety,<sup>[18,19]</sup> depression,<sup>[20]</sup> and PTSD.<sup>[21]</sup> Earlier studies suggest that different practices of yoga, such as breath control and meditation, promote good mental health.<sup>[22,23]</sup> Yoga practice maintains homeostasis in the physiological conditions, thus improving the overall well-being and quality of life.<sup>[24]</sup> Yoga practice also helps reduce the allostatic load and influences the parasympathetic activity, which directly reduces the amygdala hyperactivation and elevated cortisol levels, thus reducing stress.<sup>[25]</sup> Yoga practice also relaxes the mind by slowing the breath and focusing on present, besides shifting the sympathetic brain activity to parasympathetic system and relaxation process.<sup>[26]</sup> Practice of yoga also inhibits the sense of fear and aggressiveness and stimulates the rewarding centers of the forebrain (e.g. nucleus accumbens). It also influences other areas of the brain for bliss and pleasure. This leads to reduction in anxiety and stabilizes the heart rate, respiratory rate, blood pressure, and cardiac output. Along with reduction in stress hormone, good hormone-like  $\beta$ -endorphin is found to be increased with yoga.<sup>[27]</sup>

Studies have shown that people living in warzones are prone to mental health problems which compromise their quality of life and this cannot be alleviated with only pharmacological interventions.<sup>[28,29]</sup> Worsening quality of life leads to mental disorders which further increase

the risk of dementia and AD later in life, thus requiring other interventions to prevent the development as well as health expenditure on such disorders. These may include psychotherapy and psychoeducation which are widely used. However, these interventions can only provide psychological improvement, whereas stress and depression exert its effects not only on the psychological level but also at the endocrine and molecular level. Yoga-based research, which is in its infancy, might provide clues if it can bring the needed psychological and neuroendocrine benefits and mediate alleviation of stress. Hence, studies that examine specific population exposed to warzone stress may not only benefit such population but also generate useful data for understanding the key mediators or markers of prevention.

Hence, the present review evaluates the mental health conditions of locals and veterans in war-affected areas and whether this makes them prone to stress, depression, anxiety, and PTSD later, resulting in the development of dementia and AD. This review further discusses the existing rehabilitative framework and whether it can be modified for better management and prevention of such disorders, such as stress and trauma, in population exposed to war-related conditions. We propose evidence-based mind-body interventions in the prevention and management of these disorders through its effect on the biochemical and neuroendocrine profile of biomarkers of mental health.

To understand the current updates and gaps, studies related to the mental health in the warzones were searched through online databases such as PubMed/Medline, Scopus, and Google Scholar. Further, studies describing mental health issues pertaining to the development of dementia and AD were searched. Ongoing and failed clinical trials in development of drugs for these disorders were also cited. To gain insights into yoga-based intervention for these mental disorders, randomized, nonrandomized, controlled, noncontrolled yoga and mindfulness-based trials for war-associated mental health issues were cited in this scoping review. Based on this search, the need for examining the molecular and neuroendocrine effect of yoga intervention in the war-related mental health conditions has been suggested for researchers.

### **Extent of Stress, Anxiety, Depression in War-Prone Areas**

War adversely affects both combatants and noncombatants of the war-prone areas. Currently, countries including Afghanistan, Iraq, Nigeria, Somalia, South Sudan, Syria, and Yemen are facing conflicts and humanitarian crises. In 2005, the WHO estimated the prevalence of psychiatric disorders among people affected by the humanitarian crisis, which highlights the need for rehabilitative practices for the people living under crisis conditions.<sup>[30]</sup> The psychological and physical effects of war and conflicts cannot be eliminated from the survivors. The conflict-associated

psychosocial stress can cause neuroendocrine and immune system modulation.<sup>[28,29]</sup> War survivors show a significant lifestyle, behavioral and emotional changes leading to various mental health disorders<sup>[31]</sup> and this can also adversely affect the health conditions of the future generations<sup>[32,33]</sup> due to the epigenetic changes in the hypothalamic-pituitary-adrenal (HPA) axis.<sup>[34,35]</sup> This creates a growing interest in the mental health subjects, affected by conflicts of humanitarian crisis, and provides an opportunity of proposing an intervention studies that impact the HPA axis and neuroendocrine system. The wide variation in the prevalence rate of mental disorders in people across different areas of conflict is depicted in Table 1. Psychiatric

epidemiological research in conflict-affected areas typically exhibits varying results, with extremely high statistical heterogeneity.<sup>[41]</sup> This might be due to differences in the study designs and innumerable factors affecting the experience and expression of mental distress in this population. A report has shown that during armed conflicts, the humanitarian crises of the native population are equal to those of army personnel.<sup>[51,57]</sup> Wars and conflicts between the countries are harmful and hazardous for civilian's mental health. In the conflict-affected states, people were constantly affected by psychological, emotional, and other personality crises, due to armed conflicts and associated circumstances for the last two decades.<sup>[58]</sup> Such stressful

**Table 1: Representation of the prevalence of anxiety, depression posttraumatic stress disorder, and later development of dementia population exposed to war related conditions**

Pathology	Worldwide prevalence rate (percentage) of anxiety, depression, PTSD, and dementia in population exposed to war-related conditions	Citation
Depression	51% in Cambodians	[36]
	42% in Yugoslavians, Turkish, and Iraqi	[37]
	40% in Southeast Asians	[38]
	38.9% in Kurdish and Vietnamese	[39]
	38.8% in Guatemalan	[40]
	34.3% in Yugoslavians	[41]
	31.7% in Bosnians	[42]
	29.3% in Afghans, Iranians, and Somalis	[43]
	23% in Somalis	[44]
	20.8% in Vietnamese	[45]
	16% in Sudanese	[46]
	8.8% particularly in Vietnamese	[47]
	Anxiety	88% in Cambodians
54.4% in Guatemalan		[40]
45% in Cambodians		[36]
40.5% in Bosnians		[42]
35% in Southeast Asians		[38]
27.7% in Afghans, Iranians, and Somalis		[43]
25.0% in Kurdish and Vietnamese		[39]
PTSD	20.3% in Vietnamese	[45]
	75.4% in Sri Lankan Tamils	[49]
	66.6% in Bosnians	[42]
	44.2% in Yugoslavians, Turkish, and Iraqi	[37]
	37.8% in Somalis and Rwandans	[50]
	33.1% in Yugoslavians	[41]
	31.3% in Kurdish and Vietnamese	[39]
	22.2% in Somalis	[51]
	14% in Southeast Asians	[38]
	13% in Sudanese (Australia)	[52]
Dementia	11.8% in Guatemalan	[40]
	10.6% in Afghans, Iranians, and Somalis	[43]
	During follow-up, 17.2% of war veterans were ascertained to have newly diagnosed Dementia in US	[53]
	13% of PTSD population developed dementia in a study in Italy	[54]
	War veterans with PTSD had higher prevalence of dementia in comparison to veterans without PTSD, Houston, Texas	[55]
	PTSD was associated with increased risk of dementia over an 8 years of follow-up and two-fold higher risk of developing dementia in those with both depression and PTSD, in San Francisco, USA	[56]

PSTD=Posttraumatic stress disorder

conditions highlight the importance of carrying out studies that examine the effects of mindfulness and yoga, because studies have shown the positive effects of yoga practices in stress.<sup>[59,60]</sup> However, it cannot be ignored as mentioned in a WHO study, such studies required to be double blinded and should also include molecular and neuro endocrinal assessments in order to analyze the prevalence of depression, anxiety and PTSD.<sup>[30]</sup> Therefore, in such studies along with questionnaire based self-reported assessments additional biomarkers assessment has to be added. Molecular assessment can not only underline the severity of the condition but also enable screening the outcomes of an intervention.

### Conversion of War-Related Stress, Anxiety, and Depression to Dementia or Alzheimer's Disease

Traumatic events experienced any time in life can have a lasting mental health effect characterized by depression, anxiety, and PTSD.<sup>[43]</sup> Table 2 shows studies from various countries with war-related mental health conditions. In 2019, an estimation of mental disorders in the war conditions found that 22.1% of the conflict-affected population is affected by depression, anxiety, PTSD, or other neurological disorders at any time point.<sup>[30]</sup> A study on stress in military volunteers found progressive deterioration in cognitive function during stressful combat-like training (e.g. reaction time and vigilance,

memory, and logical reasoning) compared to baseline prestress function.<sup>[68]</sup> High prevalence of mild cognitive impairment (MCI) and dementia is also reported in military personnel who are continuously exposed to stressful environment in the war zones.<sup>[69]</sup> Due to development of mental health conditions such as stress, depression, anxiety, and PTSD in a war-affected population, there are chances of conversion to dementia and AD-like disorders.

Studies have also shown that history of depression and PTSD further increases risk of dementia.<sup>[66,67]</sup>

The underlying reasons of conversion of PTSD to dementia are not clear; however, several symptoms of PTSD such as sleep impairment<sup>[70]</sup> may contribute to reduction in hippocampal volume and abnormal protein processing besides the accumulation of amyloid-beta (A $\beta$ ), tau, and hyperphosphorylated tau,<sup>[71,72]</sup> which are the signs of dementia and AD.

Stress leads to activation of noradrenergic pathways which stimulate the release of cortisol via HPA axis activation, and hence, under stress and depression, the serum and cerebrospinal fluids levels of cortisol are elevated. The elevation in levels of cortisol may increase A $\beta$  brain burden which may consequently induce cerebral AD pathology.<sup>[65]</sup>

As the mechanisms of how stress and PTSD lead to

**Table 2: Studies from various countries, population of which has stress, posttraumatic stress disorder, depression, anxiety, dementia etc., due to exposure to war related conditions**

War prone regions	Aim of the study	Outcome of the study	Citation
Iraq	PTSD and HTQ were administered for the caregiver and the oldest child of the family	PTSD was reported in 87% of the children and 60% of their caregivers	[61]
Syria	To examine the prevalence of PTSD and to explore its relation to socio economic variables among Syrian refugees	71% of them had PTSD in the sample, which shows that PTSD is an important health issue among the Syrian refugees	[62]
Afganistan	National estimates of Afghan population aged 15 years or above	67.5% of the total recruited population had symptoms of depression. Symptoms of PTSD, anxiety, depression were high in the overall survey	[63]
Libya	Prediction of the impact of conflict in the country on the population	The proportion of comorbidity of PTSD with depression among general population was estimated to be around 50%	[64]
India	Study amongst the victims of bomb blast in Jammu and Kashmir area of the country	35.4% of the victims reported psychiatric morbidity. Psychiatric diagnosis reported that 12.9% had PTSD, 9.6% had depression and 6.4% had dissociative amnesia	[65]
Palestine	Study conducted on children from 10–19 years of age for the prevalence of PTSD	32.7% children suffered from PTSD, 49.2% from moderate PTSD, 15.6% mild PTSD and 2.5% had no signs of PTSD	[2]
Pakistan	Prevalence of PTSD, anxiety and depression in Pakistani workers who had been exposed to terror attacks	Around 15% of them showed PTSD and about 11%–15% reported high levels of depression and anxiety	[66]
Kuopio, Finland	Study conducted on men who had experienced childhood stress due to emigrating from war areas and other reasons	A positive correlation of childhood stress with late life dementia was found	[67]

PSTD=Posttraumatic stress disorder, HTQ=Harvard trauma quest

dementia or AD are not clearly understood (other than HPA axis involvement), it is attractive to analyze the neuroimmunological effectors in PTSD and dementia in a defined war-affected population making it ideal to examine. It is well known that there is increasing incidence of wars and conflicts in the world. It may render the local population and the armed forces to dementia and AD later in life. This raises the importance of nonpharmacological and cost-effective rehabilitative therapies, including yoga and mindfulness. It has been postulated that yoga acts by alteration of HPA axis and sympathetic nervous system, thus reducing the stress-induced hormonal activation.<sup>[73]</sup> Thus, yoga and mindfulness might be useful not only in the management of stress, PTSD, and depression but also an early prevention of dementia and AD in the war-affected population and affected military personnel.

Yoga and mindfulness have not been identified as a rehabilitative intervention for this population due to lack of studies describing the effects and benefits of yoga for war-related mental health conditions. Furthermore, very limited molecular studies in the field of yoga have been conducted in the context of stress, depression, PTSD, MCI, and dementia. This highlights the need of more studies on homogenous populations which could generate evidence whether yoga and mindfulness can be useful as a rehabilitative and preventive intervention such as war-related mental health and PTSD.

### Failure of Pharmacological Drugs for Treatment of Dementia and Alzheimer's Disease

Current treatment strategies are widely believed to provide symptomatic and limited relief in AD, dementia, and MCI pathologies.<sup>[70]</sup> As the current pharmacological research is based on the reductionist and whole-person approach in the field of stress and dementia,<sup>[71]</sup> repeated failure in developing pharmacotherapeutics in such complex disorders has raised questions about the efficacy of existing drugs used to treat AD and related dementia.<sup>[72]</sup> Currently, the FDA has approved a few drugs for cognitive improvement in the AD patients. These medications include choline esterase inhibitors such as donepezil and galantamine. These drugs, however, provide only symptomatic relief and have their side effects.<sup>[73]</sup> Donepezil and galantamine have been found to be helpful in neurological functions in patients with poststroke cognitive impairment but have not been shown to alter the neuroendocrine system.

Besides, most of the drugs have not been accepted for the treatment of dementia due to associated side effects and limited efficacy. Nimodipine has been found to have a short-term effect on cognitive function but not for AD or vascular cognitive impairment.<sup>[74]</sup> However, a review has compiled studies in which patients with MCI and dementia have shown improvement in cognitive function when yoga is provided as a primary or as a part of the

multicomponent intervention.<sup>[75]</sup> There were limitations with the above-mentioned yoga studies that lacked details of the interventions, including variability in the frequency/duration and components of the yoga interventions.<sup>[75]</sup>

Accumulation of amyloid has remained unaltered even with the discovery of drug solanezumab, which targets the amyloid plaques, considered as a pathological hallmark of AD.<sup>[76]</sup> It has failed in a clinical trial led by Lilly. Lilly announced a major change to its closely watched clinical trial for the Alzheimer's drug solanezumab (which binds with  $\beta$ -amyloid), which failed to show statistical significance in offering relief in the symptoms of AD.<sup>[77]</sup> All the above-mentioned treatment paradigms fundamentally target a molecule and inhibit the downstream signaling involved in AD. Disease pathology of MCI and AD is much more complex than genetic disorders, and therefore, the reductionist approach is often argued as inappropriately applied to alleviate cognitive impairment in such disorders of the brain. Table 3 describes the repeated failure of drugs for AD from time to time.

### Yoga as an Intervention to the Population of War-Prone Regions

Rehabilitation for the war-affected people is important to bring positive change in the quality of life and reduce the cognitive decline, besides preventing various lifestyle disorders.<sup>[84]</sup> Although yoga is a well-studied and re-emerging mind-body technique in stress management, there is a major gap in studies that have investigated its impact on the war-affected people through molecular assessment. A study by Carter *et al.* found a significant reduction in PTSD score in Vietnamese veterans after 6 weeks of SKY intervention. The assessment was done using Clinician-Administered PTSD Scale.<sup>[85]</sup> Another study by Gordon *et al.* was conducted on the Palestinian adults in Gaza to determine the effects of mind-body skills group (MBSG) on symptoms of PTSD, depression, and quality of life among these adults. After 10 sessions of MBSG included meditation, guided imagery, breathing techniques, autogenic training, biofeedback, genograms, and self-expression through words and drawings. The levels of PTSD, depression, and quality of life were assessed in 92 Palestinian adults with PTSD. Immediate improvement in the symptoms of PTSD, depression, and improvement in quality of life was observed. After 10 months, all these improvements remained persistent among the participants.<sup>[86]</sup> A systematic review conducted by Cushing *et al.* analyzed the studies about the impact of mind-body therapy such as meditation, yoga, and mindfulness in the post-9/11 veterans with PTSD, which showed significant improvement in PTSD symptoms in these interventions.<sup>[87]</sup> Table 4 shows the studies where yoga intervention has improved the mental health of the war-affected people. However, none of these studies examined the effects of mind-body practices at the molecular, cellular, and neuroendocrine level. In addition,

**Table 3: Failure of drugs in the clinical trials for neurodegenerative diseases**

Name of the drugs	Phase of trail fail	Years	Reasons	Citation
A $\beta$ antigens (AN1792; active vaccination)	Phase I	2006	Clearance of amyloid plaques was observed but it did not prevent progressive neurodegeneration	[78]
Tarenfurtil, the R-enantiomer of the NSAID, flurbiprofen	Phase III	2008	Failed to penetrate the blood–brain barrier in enough concentrations	[79]
Tramiprosate	Phase III	2009	No consistent improvement in cognitive performance	[80]
Solanezumab	Phase III	2012	Lack of efficacy in improving the primary outcomes, i.e., cognition and function	[81]
C-terminal anti-Ab. antibody ponezumab	Phase II	2010	No efficacious results were found	[82]
Aducanumab	Phase III	2019	No data available	[83]

Phase I clinical trial aims to examine the safe dosage of a drug with the few or no side effects. The drug is tested in a small group of 15–30 patients, Phase II trials aims to the further safety if a drug has efficacy. Phase II trials are in larger groups of patients compared to Phase I trials, Phase III trials compare a new drug to standard care of drug. These also assess the side effects of any drug. Phase III trials enroll more than 100 patients, Phase IV trials test new drugs approved by the FDA. FDA=Food and drug administration, NSAID= Nonsteroidal Anti Inflammatory Drugs

**Table 4: Several mind–body techniques administered to the war-affected people as an alternative intervention for reducing stress-induced cognitive problems and other associated factors**

Affected areas	Intervention	Aim of the study	Outcome of the study	Citation
Kosovo	MBSG	To determine whether MBSG program decreases symptoms of PTSD in war-traumatized high school students	Students in the intervention group had significantly lower PTSD symptom scores than those in the wait-list control group	[86]
Palestine	MBSG program	To assess the effectiveness of 10 session long MBSGs program for PTSD, depression, anxiety, and QOL to war-traumatized Palestinian adults	Intervention group showed significant reduction in PTSD, depression, and anxiety symptoms and QOL improvement, and maintained at 10 months of follow-up	[86]
Congo	TM	To assess whether TM practice can reduce PTS symptoms in Congolese refugees	TM practice significantly reduced PTSD symptoms in these refugees	[88]
Gaza	Mind body skills	Assessment of symptoms of PTSD and depression on hopelessness children and adolescents in Gaza	After 7 months of follow-up, improvements in total PTSD and depression score were largely maintained and decreased sense of hopelessness was maintained despite ongoing violence and economic hardships	[9]

MBSG=Mind–body skills group program, TM=Transcendental meditation, QOL=Quality Of Life, PTSD=Posttraumatic stress disorder, PTS= Post Traumatic Stress

these studies included a smaller number of participants.

### Yoga versus Psychosocial Interventions in Prevention for Mental Health Problems Such as Stress, Anxiety, Depression, Mild Cognitive Impairment, and Dementia

Yoga combines physical activity with mindful practices and breath control. Meditation is typically performed regularly with an aim to achieve homeostasis via regulation of various neuroendocrine and regulatory mechanisms.<sup>[89,90]</sup> Several systematic reviews and meta-analyses have demonstrated that yoga is effective in ameliorating symptoms of depression across a range of different clinical disorders, including mild dementia.<sup>[91,92]</sup>

A meta-analysis has investigated the effects of yoga practice on physiological markers of stress and has found that studies including yoga practice showed improved regulation

of sympathetic nervous system and HPA system.<sup>[93]</sup> Yoga is known to improve autonomous nervous system<sup>[94]</sup> and HPA axis, with consequent reduction in cortisol,<sup>[95]</sup> blood pressure,<sup>[96]</sup> heart rate,<sup>[97]</sup> fasting blood glucose, cholesterol, and low-density lipoprotein,<sup>[98]</sup> which are the biomarkers associated with conditions of chronic stress. Yoga is also known to improve sleep,<sup>[99]</sup> which is one of the related risk factors for PTSD.<sup>[91]</sup> It has been found that yoga practice through regulation of sympathetic nervous system and HPA axis reduces the conditions of depression and anxiety.<sup>[100]</sup> Similarly, yoga also improves mental well-being.<sup>[101]</sup> However, none of these reports have led to further attempts to examine the same in the vulnerable population of warzones that suffer from constant stress.<sup>[2]</sup> Li *et al.* reviewed yoga and mindfulness-based studies to examine its efficacy in reduction of stress and anxiety, they found that, out of 35 human trials, 25 showed promising results however, the limitations of these studies were

smaller sample size and lack of control group a which could be a reason of non conclusiveness of the studies.<sup>[102]</sup> A clinical trial assessed the effects of SKY in comparison to electroconvulsive therapy and imipramine on 45 untreated melancholic depressive participants, who were randomly divided; however, all three groups showed significant reduction in depression scales, but SKY group showed better scores as compared to the other groups. To conclude that SKY can be a potential alternative to drugs in melancholia as a first-line treatment,<sup>[103]</sup> such studies should be designed as randomized control trails which include molecular and neuroendocrinal estimation. A review has also compared yoga with aerobic exercise for health-related quality of life (HRQoL) and multiple physical functions in older adults. The meta-analysis revealed significant results favoring yoga group in comparison to inactive control and active control groups with overall improvement in multiple physical function and HRQoL outcomes.<sup>[104]</sup> Some other studies have compared psychological aspects in long-term meditators in comparison to novices or no meditation practitioners and have found meditation to show overall improvement in psychological aspects as compared to nonmeditators.<sup>[105-107]</sup>

Yoga-based studies have shown positive results but lack robust study designs, smaller sample size, no randomization and blinding, etc., Furthermore, very few yoga-based studies provide sufficient information regarding the yoga intervention, compliance, and the proportion of time spent practicing each of the its components (i.e. *Asanas*, *Pranayama*, and *Dhyana*), partly due to the dissociation of basic scientists from yoga practitioners and partly due to absence of quality assurance programs that govern compliance in yoga intervention studies. Such quality assurance programs are often done in research laboratories and it is called good laboratory practice,<sup>[108,109]</sup> and such practices are absent in yoga research. Few studies from reputed research groups show adherence to quality assurance principles.<sup>[110-112]</sup> All these limitations make yoga and meditation practices unrecognizable in the global scientific fraternity. Hence, limited studies that have tried to use these interventions for the much-needed population in the warzones, and the veterans from the war areas need to be supplemented by multicenter studies. Additional planned studies analyzing not only the psychological aspects but also the biological aspects of yoga on this population would not only help this population to cope with the circumstances but also help develop an understanding about the biological aspects of yoga and meditation, which has been studied to a limited extent. Table 5 shows that yoga-based interventions have helped in improvement of depression, anxiety, stress, and dementia. The studies mentioned in Table 4 could be used as reference studies for warzone populations as these yoga-based protocols have shown promising results.

## Role of Neuroendocrine System in Alleviation of Stress and Dementia by Mindfulness Approach

Experience of a traumatic event can lead to the long-term consequences on mental health along with cellular and molecular changes, which can cause long-term impact responsible for onset of diseases such as depression, MCI, dementia, AD, and many other related disorders.<sup>[120]</sup> Traumatic events are known to alter the neuronal morphology, function, and neurochemistry.<sup>[121]</sup> Brain-derived neurotrophic factor (BDNF) is actively involved in the regulation of neurogenesis. A low level of BDNF has been found to be involved in the pathophysiology of depression,<sup>[122]</sup> anxiety,<sup>[123]</sup> and dementia and Alzheimer's like syndromes.<sup>[124]</sup> BDNF reduction is associated with stressful life events, but it increases after physical training.<sup>[125]</sup> Yoga practice along with its positive impact on quality of life<sup>[24]</sup> has shown to increase BDNF levels.<sup>[126]</sup>

Sociocultural background also has an important aspect in the psychological problems of traumatized individuals.<sup>[127]</sup> A 2005 study has reported the association of low socioeconomic status with the higher vulnerability to develop PTSD and low capacity to cope with symptoms of PTSD.<sup>[128]</sup> Another 2011 study from the US has reported lower prevalence of minority people to seek treatment for PTSD than majority population, with less than half of the minority individuals taking treatment,<sup>[129]</sup> which again emphasizes the importance of awareness among different sociocultural groups. Another study has reported that direct impact of socioeconomic and cultural factors has major role in understanding psychological problems of traumatized individuals with a direct impact on the social functioning ability.<sup>[127,130]</sup>

In addition, depression and stress-like syndromes are characterized by the central and peripheral release of various markers of inflammation such as interleukins,<sup>[131]</sup> e.g., IL-6, IL-2, TNF, which are reported to be higher in depressed subjects than in non depressed subjects.<sup>[132]</sup> However, physical exercise reportedly influences the immune system and expression of its related molecules. Various inflammatory cytokine levels are reported to change during and after exercise (including IL-1 and IL-6),<sup>[133,134]</sup> some of which are directly related to pathologies related to stress.<sup>[135]</sup> The practice of yoga has also shown to reduce inflammatory cytokines.<sup>[136]</sup> Yoga can improve the antioxidant levels<sup>[137]</sup> and has also been shown to alter the levels of biomolecules associated with stress, including cortisol, IL-6, beta-endorphins, sirtuin-1, and BDNF.<sup>[138]</sup> Studies have shown that mind-body interventions can modulate the inflammatory gene expression induced with persistent stress conditions.<sup>[139]</sup>

During past few years, yoga is being recognized in the prevention and management of stress, depression, anxiety, MCI, and related disorders, but not many studies have been carried out to correlate the physiological outcome with molecular markers induced by yoga in relation to these disorders.

**Table 5: The list of some yoga protocols used across the world for the management of anxiety, depression, stress, and dementia which are also the health problems faced by people exposed to war related conditions**

Name of protocol	Protocol	Effect	Reference
Iyenger yoga and coherent breathing	90 min=yoga postures, transition and deep relaxation followed by coherent breathing	Reduction in depressive symptoms after 12 weeks of Iyenger yoga and coherent breathing intervention	[113]
Yoga breath intervention	8 h program=4 days 2-h four breathing techniques, chanting 'OM' and SK	Relieved psychological distress in treatment group compared to control group after 6 weeks of the intervention	[114]
Multicomponent yoga breath Program	Modified Sudarshan Kriya Yoga Nidra (yogic sleep) Breathing techniques Chanting "OM" Alternate nostril breathing	Provided significant improvement in population with severe PTSD, alcohol abuse, and dependence on disability status	[85]
A yoga stress reduction intervention	90-min yoga protocol includes Conceptual grounding Breathing Postures Meditation	Significant improvement in perceived stress, psychological, behavioral, and physical symptoms of stress after 10 weeks of yoga intervention	[115]
Kundalini yoga	60-min Kundalini yoga 12-min home practice of Kirtan Kriya meditation	Kundalini yoga improves executive functioning, depressed mood, and resilience with greater and sustained improvement in mood compared to memory enhancement training group	[116]
A yoga program for cognitive enhancement	Seated mindfulness scan and set positive affirmation Final relaxation: Guided mindfulness meditation	An improvement in working memory functioning and enhance attentive mindfulness after 6 yoga sessions	[117]
Yoga for memory enhancement training, in patients with clinical dementia rating scale score (<0.5)	The content and structure of the class including Kundalini yoga session 1) Tuning in (5 min) 2) Warm-up (10 min) 3) Breath techniques "Pranayama" (10 min) 4) Kriya (20 min) 5) Meditation (11 min) 6) Rest "Shavasana" and closing (4 min)	After 12 weeks of yoga effective improvement in verbal memory was correlated with increased functional connectivity in brain networks	[118]
Yoga for physical and mental health of elder adults with dementia	Warm up (20 min) Hatha yoga (20 min) Relaxation (10 min)	12 weeks of yoga training program improved physical and mental health than nonparticipating group. Further, the depression state and problem behaviors were also significantly reduced	[119]

SK=Sudarshan Kriya, PTSD=Posttraumatic stress disorder

Furthermore, the molecular changes leading to these disorders have not been explored in the warzone population being highly prone to these disorders. Therefore, it is imperative to analyze the biochemical, molecular markers related to pathways of inflammation, angiogenesis, and neurogenesis, which are directly affected with the above-mentioned disorders. During the past few years, mind-body intervention is gaining interest as it has been found to be beneficial in reducing stress, depression, anxiety, MCI, and related chronic diseases, but again comparative studies are still lacking.

Hence, employing study designs based on yoga protocols in warzones and paramilitary barracks can provide insights about the molecular and sociocultural impact of yoga

besides improving management of the mental stress among this population.

### Recommendations for Future Research

The higher probability of disorders such as stress, anxiety, depression, dementia, and AD in the locals of war-prone areas and the army combats have been well defined in the literature. Yoga is proposed as an intervention for the vulnerable population. However, very few studies have been devoted to investigating the efficacy of yoga on the war combatants and war-exposed civilians and PTSD-related conditions. In this review, several new research questions were identified. For example, what is the extent of



war-prone–related anxiety, depression, in war-prone areas, and if these convert to dementia? Are mind–body techniques acceptable to such vulnerable populations? Could yoga intervention be superior to other psychosocial interventions for mental health issues confronted by such a population? Can yoga prevent progression of stress and dementia into AD? What is the role of neuroendocrine system in alleviation of stress and dementia by mindfulness approach? Much more data are required to not only understand the benefits and barriers in implementing such techniques but also bridge the chasm of knowledge and practice of mindfulness-based yoga. Can practicing these techniques reduce PTSD among individuals immediately after war trauma and in the war-prone area? For advancing our understanding further, the benefits of yoga as an intervention need analysis at the physiological and molecular level.

### Conclusion

Wars and conflicts affect the social and mental well-being of the individuals who are directly or indirectly involved. Residents of war-prone areas, along with the military combats, are the most vulnerable population for the war-related effects. The war-related stress may lead to development of various disorders such as depression, anxiety, stress, and PTSD and these can later lead to the development of dementia and AD. Mental health of the war-afflicted population and the military personnel has not been given much importance. They are continually exposed to such circumstances as this population is highly prone to develop various mental disorders affecting their social, emotional, and physical well-being. There are limitations in fulfillment of the mental and medical needs of this population, and evidence-based yoga and mindfulness interventions can bridge these gaps. As shown by studies, yoga not only provides anxiety related relief, but it also acts through the cell survival mechanisms, thus improving the overall health of the practitioner. Hence, inclusion of Yoga and Mindfulness in the daily routine of the military personnels and population of war afflicted areas can be helpful in the prevention and management of war related mental health disorders. For yoga and mindfulness to be adopted by the medical healthcare fraternity, there is a need to learn new methods to change health providers' attitude, by launching new studies with rigorous guidelines based on evidence generated by engagement of military forces and residents of war-affected areas before integrating them with healthcare for effective rehabilitation. This will not only help in understanding of molecular pathways of cognitive impairment and how stress alleviation is achieved by yoga intervention but also is discerning the public health model for wellness. In addition, if the medical staff/patients/families/caregivers are provided some basic, practical resources of yoga and mindful techniques, this would encourage active participation in enrollment.

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