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Review Article

Role of Yoga in Anxiety: An Updated Review on Pathological Changes in Biochemical Markers

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Abstract

The physical and mental practice of yoga is a traditional and ancient discipline for promoting right living and well-being. From fostering health management in lifestyle-related diseases to create harmony and balance in an individual's life, yoga plays a principle ethical influence. Anxiety is regarded as a fundamental term in psychoanalytic ideas concerning the dynamics of mental, physical and emotional functioning. According to the WHO reports, the post-COVID period has led to an increase in mental ailments specially anxiety, in India, particularly among adolescents. This review elucidates the role of yoga in alleviating anxiety and delineates the metabolic alterations in persons afflicted by this mental disease. The practice of Ashtanga yoga, encompassing the eight limbs of yoga, facilitates the attainment of ethical principles, contentment, spiritual discipline, mental tranquility, inner serenity, cognitive concentration, and instructs on the elimination of extraneous influences. The physiological alterations resulting from yoga practice have been documented in various case studies, clinical data, and scientific publications. The practice of yoga, when performed correctly, decreases cortisol levels (stress hormone) while enhancing the effects of gamma-aminobutyric acid, stimulating serotonin synthesis, brain-derived neurotrophic factor, dopamine, and endorphins (happy hormones). These improvements significantly reduce the impact of anxiety in individuals. Yoga serves as a significant alternative supplemental therapy for the treatment of various mental disorders, including anxiety. The molecular-level mechanisms and further scientific inquiry are of future significance.

Keywords: Yoga; Anxiety; Alternative complimentary medicine

Introduction

Anxiety is a cardinal symptom of many psychiatric disorders [1]. Anxiety is a disorderly, diffused, vexatious and a persistent state of negative emotions characterized by perturbed anticipation of unpredictable future risks accompanied by a state of hyper-vigilance. According to the Institute for Health Metrics and Evaluation (GBD 2019 study) an estimate of 4%, translating to 301 million people, of the global population suffered from anxiety, making it the most common psychoneurotic disorder with a life-time prevalence [2]. Anxiety-related problems typically manifest during childhood and adolescence and may persist if left untreated. According to the National Institute of Mental Health, young adults aged 18–25 in the US had the greatest prevalence of mental health disorders (30.6%), followed by age group 26–49 (25.3%) and 50+ (14.5%) [3]. Additionally, the global prevalence of anxiety and depression disorders increased from 196 million to 246 million during the COVID-19 pandemic [4]. In another data released by WHO, the post COVID time period also marked surge count of mental disorders occurrence in India, engulfing 9.3% of youth during the lockdown era and later increased to 16.8% by March 2022 [5,6]. Anxiety encompasses several mental health issues, with particular phobias at a prevalence of 10.3%, panic disorders at 6.0%, and psychosocial phobias at 2.7%, being the most prevalent [7]. Anxiety and related disorders are highly prevalent and are root cause of many functional and psychic impairment as shown in Figure 1.

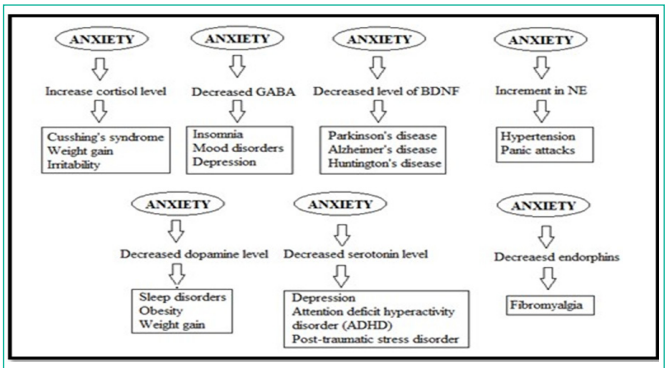

Figure 1: Anxiety and associated health risks.

The metrics reveal burgeon in prevalence, incidence and DALY rates in upcoming years producing significant threats to population's well-being and quality of life. A significant number of individuals with anxiety do not seek treatment due to a lack of knowledge and awareness, a lack of interest in mental health management, and a gap in mental healthcare facilities, which highlights the paucity of mental health professionals. A recent report conveys availability of only one mental health care provider for every 350 suffering individuals in the United States [8]. Pan American Health Organization refers anxiety as a group of mental disorders characterized by fear, generalized anxi-

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ety disorder, phobias, social anxiety disorder, obsessive compulsive disorder and post-traumatic stress disorder [9]. The prevalence of anxiety disorder is likely to enormously out-space available resources. Psychopharmacology stays as the mainstream treatment for anxiety and other neurological and psychiatric disorders till date. Nonetheless, these treatment regimens are linked to significant metabolic adverse consequences, including obesity, disruptions in glucose homeostasis, and alterations in lipid metabolism [10]. Coronary arteriosclerosis [11], hypercholesterolaemia and sexual dysfunction and anorgasmia [12]. It is imperative to integrate non-pharmacological therapies in the treatment and management of neuropsychotic diseases like anxiety. Yoga practices seem to be an ideal non-pharmacological remedy for anxiety-related conditions, effectively mitigating the detrimental impacts of the illness by modifying sympathetic-parasympathetic and neuro-endocrine pathways, thereby restoring neuro-immunological homeostasis in individuals. Yoga is an ancient discipline encompassing the physical and mental practices of right living and wellness. The term "Yoga" stems from the Sanskrit word "yuj," signifying "to join," "to unite," or "to yoke," representing a comprehensive approach to the integration of individual inner consciousness with the universal or cosmic spiritual conscience [13]. As defined by Maharshi Patanjali, "*yogaḥcittavṛttinirodhaḥ*"; the skill and practice of yoga is demonstrated by deliberate non-operational modes of mental and emotional vibration frequencies. The philosophical roots of yoga originate from ancient India over 2000 years ago [14]. It is a state of self-realization and liberation. It is a multi-modal discipline indoctrinating consciousness. The art and practice of yoga is a mind body intervention which aims at bringing harmony and balance in an individual's life and promote health management in lifestyle-related disorders. Yoga has become a popular approach for improving mental and emotional wellbeing. A large population experiencing anxiety related disorders do not seek medical or therapeutic intervention and rather choose self-management. The prevalence and increasing global burden of anxiety suggests the need of critical contemporary approaches such as yoga to be systematically meta-analyzed in patients with anxiety and related disorders. The aim of this review is to assess and indicate the role of yoga and associated changes in biomarkers exterminating the symptoms of elevated levels of anxiety or related disorders in suffering individuals.

Limbs of Yoga

According to Patanjali, a well-known Hindu author and philosopher, the "Yoga Sutra" provides a taxonomy of yogas. Patanjali mentions eight limbs of yoga, which are often referred to as "Ashtanga yoga." The limbs are *Yama* (Abstention), *Niyama* (Observances), *Asana* (Postures), *Pranayama* (Breath control of Prana), *Pratyahara* (Sense withdrawal), *Dharana* (Concentration), *Dhyana* (Meditation) and *Samadhi* (Contemplation) [15]. *Yama* deals with moral code, honesty, integrity, pointing on individual's behavior and how individual deals with their own lives. There are five *Yama* like *Ahimsa* (non-violence), *Satya* (truthfulness), *Asteya* (nonstealing), *Brahmacharya* (continence or celibacy) and *Aparigraha* (non-covetousness) [16]. Engaging in these five disciplines enhances an individual's capacity for low-stress tolerance, hence alleviating anxiety and sadness [17]. *Niyama*, also considered as personal disciplines, comprises of *Saucha* (Cleanliness/Purification), *Santosa* (Contentment), *Tapas* (Spiritual asceticism), *Svadhyaya* (Study of sacred scriptures) and *IshvaraPranidhana* (Dedication/surrender to Almighty) [18]. The purify mind, happiness, spiritual austerity and the devotion to God help ones to minimize his/her ego function, get increment in behavioural control in odd situation and in reducing mental anxiety. [17] The yogic limb, *Asana*, indicates the comfortable posture to attain the mental relaxation and it is associated with breath-work. This practice improves the body postures, flexibility and blood circulations [19]. *Pranayama*, which is related to breathing practice with inhalation and exhalation with proper pause, is not only removing toxins from the body, but also releases the mental knots by the increment of inner peace, joy and creativity [20]. The term *Prtyahara*, the next practice of yoga, indicates avoiding or controlling of wrong food or external influences. To get rid of anxiety *Prtyaharahas* a great impact [21]. *Dharana* signifies mental focus, concentration, and introspection. The practice of the sixth limb of yoga fixes the mind by maintaining a single, focused attention without daydreaming or hopping from one subject to another [22]. Techniques for *Dhyana* (Meditation) may involve certain body alignments, concentrated attention, or a non-judgmental approach to interruptions. They are used by people to promote overall health and well-being, promote psychological equilibrium, manage disease, and promote peace and relaxation [23]. Samadhi is a spiritual condition reached when the mind becomes so completely consumed with whatever it is thinking about that it loses all feeling of who it is. The practice of *Pranayama* with Samadhi is termed as *Siddha Samadhi* Yoga [18,24].

Pathological Changes in Biochemical Markers

The role and efficacy of yoga practices have been investigated and enumerated in various clinical studies. There are many possible mechanisms by which alteration in the biological pathway ultimately serves to affect the underlying pathophysiology of anxiety and related disorders. The autonomic nervous system has two components viz, sympathetic and parasympathetic system. Dysfunction of ANS (Autonomic Nervous System) is related to anxiety [25]. Anxiety activates the sympathetic cascade; the flight and fight response accompanied with physiological bodily symptoms like panic attacks, palpitations, elevated pulse rates, shallow and short-breathe, headaches, insomnia, xerostomia, uncontrollable muscle twitching and trembling. One of the well-known physiological repercussions of anxiety and related diseases is the stimulation of the hypothalamic-pituitary-adrenal axis, which releases epinephrine, also referred to as adrenaline [26]. Anxiety related disorders are also associated with other neurotransmitters, such as dopamine, GABA, and serotonin [27,28].

Yoga practices have been reported to serve the regulation of these neuro-biomarkers. *Pranayama* breathing practices of yoga seem to reduce sympathetic activity and bring about parasympathetic dominance through vagal stimulatory pathways [29]. Anxiety and related disorders seed parasympathetic suppression. Additionally, yoga has been shown to increase GABA levels and decrease parasympathetic system underactivity, both of which are linked to a better sense of wellbeing. Cortisol levels are significantly elevated in anxiety and stress. Regular yoga practice considerably lowers cortisol levels by regulating the hypothalamic-pituitary-adrenal axis (HPA). The biomarkers, pathological changes and possible mechanism have been mentioned in Table 1.

Table 1: Yogic practice and biomarkers.

Biomarker	Pathological changes due to yogic practice	Possible mechanism
Cortisol	Yogic practice can reduce cortisol levels.	By downregulating the HPA axis
GABA	Practice of yoga can increase the activity of the GABA system.	• By acting on vagal stimulation, • By decreasing the activation and reactivity of the sympathoadrenal system and the HPA axis • By activating parasympathetic nervous system
BDNF	Increment in BDNF occurs due to practice of yoga.	By vagal tone and Parasympathetic activation
Noradrenaline (NE)	Yoga lowers the level of NE.	By acting on locus coeruleus to reduce the release of NE. Activation of meditation chakra lowers the activity of locus coeruleus to release NE.
Dopamine	Practicing yoga increases the levels of dopamine.	By the activation of dopamine receptors and positive dopaminergic responses from the ventral striatum
Serotonin	Yoga enhances serotonin level.	By the reductions in monoamine oxidase (MAO) levels
Endorphins	Significant increase in endorphins causes due to yogic practice.	by activating the parasympathetic nervous system

Cortisol

The serum cortisol level serves as a recognized biomarker for assessing stress and anxiety levels. Increased cortisol levels are associated with elevated anxiety levels. Consistent engagement in yogic sessions has been shown to lower cortisol levels and, consequently, related psychological responses. Research indicates that yoga can lower cortisol levels by modulating the hypothalamic-pituitary-adrenal (HPA) axis [30-31]. A randomized controlled trial involving 58 patients with major depressive disorder revealed that a 12-week intervention focused on yoga and meditation-based lifestyles resulted in significant changes in biomarkers related to neuroplasticity and stress [32]. Several studies from last few decades emphasized that development of acute and chronic stress is mainly through involvement of hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system which not only seeds anxiety disorders but also play crucial role in dysregulation and dysfunction of immune system [33]. Yoga not only diminishes the occurrence likelihood of hypercortisolemia associated stress and anxiety but also facilitates neurotropism. The underlying mechanism may include enhancement in parasympathetic and vagal tone alongside a reduction in stimulation of *locus ceruleus* leading to decrease norepinephrine output. This, in turn, results in negative feedback to corticotropin-releasing hormone and cortisol levels [34].

Gamma Amino Butyric Acid (GABA)

One of the major reported mechanisms through which yogic sessions enhance mood and induce a sense of euphoria is through augmentation of GABA system activity [35]. Numerous evidences of biological mechanisms have suggested that yoga influences GABA system activity which contributes to the therapeutic efficacy of vagal nervous system (VNS). This modulation reduces the activation and reactivity of the sympathoadrenal system and the HPA axis, resulting in parasympathetic activation and a transition from sympathetic to parasympathetic activity, thereby diminishing the release of stress hormones [36]. In a recent study, it was assessed that a 12 week of 90 minutes yoga protocol practice upon patients with major depressive disorders, which included 60 minutes of Iyengar yoga, 10 minutes of relaxation and then 20 minutes of coherent breathing exercises with equal inhalation and exhalation resulted in improved thalamic GABA levels. During the study it was also observed that such elevated GABA levels did not sustain after 8 days of discontinuing selected yogic sessions. Hence, yoga needs to be a regular practice to maintain elevated GABA levels [37].

Through the practice of yoga, the parasympathetic nervous system is activated, leading to a relaxation response, reversing the effects of the sympathetic nervous system and the fight-or-flight response [38]. It is postulated that the clinically noted positive effects of yoga such as improvement in mood, reduction in anxiety, subjective feeling of 'connectedness' and enhanced social cognition may be driven by its influence on the interactive and inter-dependent relationships between GABA, oxytocin and cortisol [39]. Few preliminary research involving healthy individuals has shown the influence of yoga on various neurotransmitters and hormones, including an increase in β-endorphins, a reduction in catecholamines, and an elevation in dopamine levels associated with intense meditation [40-43].

Brain-Derived Neurotrophic Factor (BDNF)

BDNF is a neuro-regulatory, brain derived neurotropic factor which plays pivotal role in neuroplasticity of the central nervous system and regulate sensory neurotransmission at both reflex and brain levels. A reduction in BDNF has been associated with development of anxiety and associated psychic disorder [44]. It has been exhaustively studied that yogic postures and exercise interventions elevate BDNF levels subsequently enhancing serotonin signaling. This mechanism is recognized as a significant contributor to the beneficial effects of yoga on mental and neurological disorders [45].

Norepinephrine (NE)

NE serves as an additional biomarker associated with anxiety. The locus coeruleus (LC), a nucleus situated in the pons region of the brainstem, is posited to harbor the highest concentration of norepinephrine. A multitude of studies has demonstrated that an augmentation in this area of the brainstem correlates with anxiety. Chronic exposure to stress-inducing stimuli results in heightened responses and increased activity, accompanied by the onset of anxiety and associated behavioral patterns [46]. Stressful events stimulate the brainstem nuclei of the locus coeruleus, which possesses a significant number of norepinephrine projections throughout the central nervous system. The activation of the locus coeruleus results in the release of norepinephrine. A study indicated that rats exhibiting limited norepinephrine release displayed a subdued response to stimuli that induce fear and stress [47]. A comparative study examining norepinephrine levels in two distinct groups of heart failure patients revealed that the cohort engaged in meditation and yogic practices exhibited markedly lower plasma norepinephrine levels than their counterparts who participated in weekly meetings [48]. An analogous experimental investigation further indicated that individuals engaging in transcendental and sidhi transcendental meditation practices demonstrated reduced levels of NE [49]. The findings suggest that a reduced level of NE correlates with a diminished occurrence of anxiety.

Dopamine

Engaging in yoga practice elevates dopamine levels. A multitude of studies presents evidence that yoga and meditative practices enhance the dopaminergic response within the body. Evidence indicates that dopamine is crucial in alleviating anxiety by activating and producing favorable responses from the ventral striatum (nucleus accumbens), a subcortical area of the brain rich in dopaminergic neurons. A recent investigation has substantiated that, 11C-raclopride, a D2/D3 receptor antagonist, binding in ventral striatum declined by 7.9% while practicing yoga and meditation and in turn corresponded to 65% elevation in release of endogenous dopamine which is related to concomitantly reduced stress and anxiety occurrence [50].

Serotonin

The "serotonin hypothesis" posits that a reduction in serotonin pathways contributes to the pathological development of anxiety and associated disorders. Serotonin is a significant neurotransmitter that plays a crucial role in the regulation of mood and the experience of well-being. A deficiency in the pathways responsible for the production and release of serotonin is associated with the onset of depression. Several studies conducted on individuals engaging in yoga practices reveal that it fosters beneficial changes in their emotional response [51,52]. Regular practice and daily sessions of yogic postures enhances serotonin production, and reduces monoamine oxidase levels, an enzyme involved in breakdown of cortisol and thus reducing stress and anxiety.

Endorphins

Endorphins act as emotional channel between the brain, nervous system and the generated response of anxiety, fear, worry, happiness, joy and pleasure. Endorphins are said to create a sense of euphoria and play a distinctive role in the emotional aspect of pain. It is also associated with the adaptability of an individual in their social and behavioral prospects. Scientific evidence indicates that a consistent engagement in yogic practices elevates endorphin levels. A study revealed that individuals practicing yoga exhibited reduced cortisol levels and increased endorphin levels following their sessions [53].

Discussion and Conclusion

Anxiety, as a neurological condition, presents a significant challenge and risk to societal cohesion and overall well-being. Anxiety stands out as a prevalent affliction within contemporary society, among various mental health disorders. Anxiety intensifies various related conditions such as insomnia, depression, irritable bowel syndrome, substance abuse, and suicidal ideation. In the period surrounding and following the COVID pandemic, there has been a notable rise in anxiety levels across all demographics, with a particular emphasis on the youth population. Yoga, a practice with a long-standing history, serves as a complementary approach in the treatment of various mental health conditions, including anxiety.

The therapeutic methodology of yoga is distinctly and thoughtfully manifested through alterations in chemical or neurological biomarkers. The primary focus on neurotransmitters and their concentrations has been recognized as a method for the neuro-analytical examination of anxiety. Diverse methodologies are currently under examination to elucidate the fundamental mechanisms and contributions of yoga in modulating these neuro-biomarkers associated with alleviating anxiety and related psychological symptoms. The practice of yoga has been linked to reductions in cortisol levels and the promotion of anti-anxiety effects, achieved through the stimulation of vagal tone, activation of parasympathetic activity, and enhancement of neuroplasticity via the downregulation of the HPA axis, resulting in elevated BDNF levels [54]. Moreover, the activation of parasympathetic tone diminishes norepinephrine firing at the locus coeruleus, which serves as the principal noradrenergic innervation within the brainstem, thereby inducing a state of mental relaxation. The practice of yoga plays a significant role in enhancing parasympathetic tone, which subsequently facilitates the relaxation of arterial baroreceptors, thereby promoting improved GABA-ergic response [55]. The practice of yoga is associated with the activation of glutamate transmission within the medial hypothalamic region, leading to a pulsating increase in beta-endorphins [56]. Yoga enhances the production of the beneficial monoamine neurochemicals, dopamine and serotonin, by promoting their release and inhibiting the function of monoamine oxidases [57].

Consequently, yoga, as an adjunctive therapeutic modality, has the potential to reduce the financial burden associated with synthetic

pharmaceuticals. While the physiological and chemical transformations occurring within an individual's body as a result of yoga practice require further scientific exploration, this area should certainly capture the attention of future researchers in the field of yoga.

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