ISSN: 2694-1767
DOI: 10.33552/WJYPR.2020.02.000541
World Journal of
Yoga, Physical Therapy and Rehabilitation
Iris Publishers

Mini Review

Yoga and GABA: New Insights from the Science

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Received Date: September 23, 2020

Published Date: October 12, 2020

Abstract

Yoga relieves stress, as does targeted modulation of the brain's major inhibitory transmitter GABA. Yoga elevation of brain GABA is accompanied by decreased anxiety with new evidence suggesting a temporal dependency on the nature of the yoga intervention. How GABA-related brain metabolism is influenced by yoga remains to be clarified. GABA produced outside the brain by the brain-gut axis and the gut's microbiome may also be involved since they are linked to reduced emotional behavior. These latter issues and their investigation will likely provide novel insights into the behavioral benefits of yoga moving forward.

Abbreviations

GABA: Gamma-aminobutyric acid; HPA: Hypothalamic-pituitary-adrenal; MRI: Magnetic resonance imaging; PET: Positron emission tomography; PNS: Parasympathetic nervous system; SNS: Sympathetic nervous system

Introduction

GABA is a neurotransmitter of major significance in the brain, being released by up to 40% of neurones to activate chloride channels [1]. This process generally results in inhibition of neuronal firing. GABA also has an important role in brain metabolism with up to 30% of the turnover to the tricarboxylic acid cycle in brain going via the GABA shunt. So, on the numbers, it is no surprise that yoga is associated somehow with GABA mechanisms. What is the science behind this association?

The balance between inhibition mediated by GABA and excitation by L-glutamate is vital to brain function. Too much inhibition or too little excitation may be equated with depression, anaesthesia and coma. Too much excitation or too little inhibition may be equated with anxiety, hyperexcitability, epilepsy and convulsions. Yoga has been shown to influence this balance. Emerging evidence from recent clinical in vivo experiments suggests that yoga improves GABA-mediated cortical-inhibitory tone [2]. The antianxiety action of benzodiazepines is known to result from increasing the action of GABA on certain of its receptors in the brain.

Discussion

Stress

Stress is defined as a disruption of the body's homeostasis. This is usually episodic, and adaptive responses reinstate homeostasis. Prolonged stress, however, can disrupt the usual adaptive responses and have negative consequences. The autonomic nervous system is integral to the maintenance of homeostasis through balance of its parasympathetic and sympathetic arms to regulate viscera, vasculature, the heart, skeletal muscle and

control of energy metabolism. When experiencing physiological or psychological stress, the sympathetic nervous system dominates, and parasympathetic activity is disrupted. During stress, the hypothalamic-pituitary-adrenal (HPA) axis is also activated, releasing the stress hormone cortisol.

Relief of stress is a feature of yoga. There is a substantial literature on yoga and stress, often involving changes in levels of the stress hormone cortisol [3]. GABA receptors are known to be influenced by stress and steroid hormones such as cortisol [4]. Agents that are known to influence stress have been shown to act directly on GABA receptors including drugs such as benzodiazepines. Yoga has been described as a non-pharmacological alternative to benzodiazepines for the treatment of anxiety [5]. Generally speaking, increased activity of GABA results in relief of anxiety and stress. We know from studies on cloned receptors, that this benefit is achieved via increased activity of GABA receptors increasing the rate of opening and closing chloride channels. We know that specific subtypes of GABA receptors are involved.

From animal studies we know that GABA receptors are sensitive to subtle changes in the environment. These changes are sex-dependent and can be relatively rapid as well as long lasting [4]. The changes may be mediated by stress-induced changes in GABA receptor modulators, such as neuroactive steroids [6] and endogenous benzodiazepines "endozepines" [7], receptor phosphorylation and/or trafficking. It is possible that the association between yoga and GABA involves similar mechanisms.

Yoga increases GABA in the brain

Our most direct understanding of the association between yoga and GABA comes from the work of Streeter and colleagues. They used magnetic resonance spectroscopy to measure GABA levels in the brain. In an early study they compared the effect of a 60-minute yoga session by yoga practitioners with a 60-minute reading session by comparator subjects on brain GABA levels. They found a significant 27% increase in brain GABA levels following 60 minutes of yoga compared to baseline (pre-yoga session) but no change from baseline in the comparator group [8]. In another study, participants who undertook twelve weeks of yoga (60 minutes three times a week) demonstrated greater improvement in mood and reduction in anxiety compared with subjects who participated in twelve weeks of walking (60 minutes three times a week [9]. Yoga was also associated with increased GABA release in the thalamus as measured by MRI, and this increase was correlated with improved mood and reduced anxiety [8]. They recently extended these studies to show a 12-week Iyengar yoga and coherent breathing intervention (two to three sessions per week) in participants diagnosed with major depressive disorder significantly increased GABA levels in the thalamus, concurrent with an increase in mood as measured by the Beck Depression Inventory II [10]. The observed increase in GABA levels was no longer observed 8 days after yoga intervention, suggesting that at least one intervention a week may be necessary to maintain elevated GABA levels. As the authors comment, magnetic resonance spectroscopy is limited by only measuring the presence of GABA, not cellular location or receptor activity. Thus, the improvement in mood and reduction in anxiety gained from yoga may be due in part to increased thalamic GABA release. Elevation of GABA levels following acute and chronic yoga practice also points towards yoga practice as effective treatment for "low GABA states" such as depression and anxiety [8].

Where does the increased GABA come from? GABA in the brain turns over quite rapidly. If the synthesizing enzyme L-glutamate decarboxylase is blocked, it takes only some 30 minutes for the levels of GABA to drop such that convulsions occur. Conversely if the metabolizing enzyme GABA transaminase is blocked, GABA levels build up such that enzyme blockers are anticonvulsants. GABA exists in different pools in the brain that turnover at different rates and have multiple roles-transmitter, metabolite and trophic factor [11]. Thus, increased GABA associated with yoga could result from decreased metabolism of GABA or increased synthesis. Neuroimaging studies have suggested that activation of the prefrontal cortex during or after yoga may increase L-glutamate stimulating the thalamic increase in GABA [12]. A variety of neuroimaging techniques have revealed information on the regions of the brain influenced by yoga. Rather less information has been revealed about brain metabolites and neurotransmitters. A PET study has provided interesting findings on dopamine release using a 11C-probe [12]. Similar studies need to be undertaken with GABA.

Parasympathetic vagal afferents and the brain-gut axis

Increased thalamic GABA possibly could come from outside the brain via stimulation of parasympathetic vagal afferents from the thoracic and abdominal viscera synapsing back onto the central nervous system. Vagal afferent neurons originating from pharynx, larynx, trachea, thoracic and abdominal viscera synapse on the brainstem nucleus tractus solitaries, which projects to the thalamus as well as areas of the brain known to regulate stress (e.g. hippocampus and hypothalamus), responses to threat (e.g. amygdala), and autonomic and HPA axis outputs [13]. GABA interneurons and GABA receptors are integral to these brain regions, hence regulation of the stress response. Streeter et al. [13] have hypothesized that the stress-induced imbalance in autonomic function leads to underactivity of the GABA system. Yoga-based practices correct underactivity of the PNS and GABA systems in part through stimulation of the vagal afferents to synapse on key brain areas that increase GABA levels, hence reduce stress and anxiety. Since vagal tone correlates with capacity to regulate stress responses and is influenced by breathing, an increase in vagal tone through yoga maybe a basis for the mitigation of anxiety disorders [14].

GABA is extensively distributed within the enteric nervous system and is an important 'postbiotic', a metabolite of gut microbiota [14-16]. It is interesting that chronic treatment of mice with GABA-producing Lactobacilli, has been shown to reduce anxiety behaviours in the elevated plus maze and fear conditioning task [17]. Gut microbes are known to affect the brain and behaviour via the vagus [18] to influence disorders mediated by the gut-brain axis including depression and anxiety [14,15]. Based on evidence that exercise modifies gut microbiota composition contingent upon sustainment of the exercise [19,20], it is reasonable that yoga-induced alterations to gut microbiome and GABA concentrations may contribute to the GABA-elevating and stress-reducing effects of yoga practice.

Conclusion

Current evidence strongly implicates increased GABA function as a result of yoga practice as contributing to the beneficial effects of GABA through reducing stress and anxiety. However, further mechanistic insights are needed of GABA metabolism using advanced brain imaging and of how parasympathetic vagal afferents and the gut microbiome regulate brain GABA in yoga. These concepts and their advancement will strengthen the message that improved GABA function contributes to the behavioral benefits of yoga.

Acknowledgment

None.

Conflict of Interest

No conflicts of interest.

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