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## How Might Yoga Help Depression? A Neurobiological Perspective

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### Abstract

Depression is a prevalent mental health condition worldwide and is the leading cause of disability in adults under the age of 45. Most individuals with major depressive disorder (MDD) report only a 50% decrease in symptoms with the use of the standard allopathic treatments for depression. The mechanisms underlying depression remain poorly understood even though stress and its correlates contribute to multiple aspects of the phenomenology of depression. Thus, stress and depression are clearly linked, as stress may precipitate or exacerbate depressive symptoms and depression may be a cause and/or outcome of acute or chronic stress. Therefore, use of additional therapeutic approaches to address stress and depression, such as complementary therapies including yoga, may contribute importantly to symptom reduction. Based on an emerging picture of how stress and mood are regulated within the nervous system, and considering the *Executive Homeostatic Network* concept that we have recently advanced, we provide an integrative overview of biological mechanisms and substrates that may mediate depression, which should be targets for research to evaluate how the practice of yoga can mitigate depressive symptomatology.

### Introduction

Mental health disorders are among the top five most costly conditions in the non-institutionalized population in the United States,<sup>1</sup> along with heart disease, cancer, and asthma. Individuals with chronic diseases such as these often report that stress, anxiety, and depression exacerbate their condition.<sup>2</sup> Similarly, chronic disease exacerbates mental health problems. Depression, in particular, is a prevalent and debilitating mental health condition worldwide and is the leading cause of disability in adults under the age of 45.<sup>3,4</sup> Although the mechanisms underlying depression remain poorly understood, stress and its correlates contribute to multiple aspects of the phenomenology of depression. Most individuals with MDD report only a 50% decrease in symptoms with the use of the standard treatment for depression, which is generally antidepressant medications.<sup>5</sup> Thus, use of additional therapeutic approaches that can address stress, including complementary therapies such as yoga, may contribute importantly to symptom reduction. In this article, we provide an

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integrative overview of psychosocial and neurobiological contributions to stress and depression, and suggest possible mechanisms by which the practice of yoga could mitigate depressive symptomatology.

## Depression

The DSM-IV-TR characterizes major depressive disorder (MDD) as a persistent depressed mood or loss of pleasure (anhedonia) for at least two weeks accompanied by a constellation of other symptoms that may include feelings of guilt or worthlessness, cognitive slowing, changes in sleep, changes in appetite, and potential suicidal ideations.<sup>6</sup> MDD can be episodic, although the majority of individuals with MDD experience recurrences, and every recurrent episode increases the probability of another, a phenomenon known as “kindling”.<sup>7</sup> Individuals with MDD have a high rate of co-morbidity with other conditions, with anxiety being the most common.<sup>8</sup> MDD significantly affects daily functioning, such that up to 60% of depressed individuals report that the condition has a severe or very severe impairment on their daily lives.<sup>8</sup>

The interplay between stressors, the environment, and the individual’s ability to cope appears to be key factors in depression. Depression can be thought of as recuperative behavior, whereby in the context of psychological (stress) or physiological (illness) challenges, an individual withdraws from the environment in an effort to prevent further injury. Current life stresses and the individual’s appraisal of the stressors influence risk of depression; individuals who demonstrate negative affect, self-critical attitudes, and insecure attachments are at higher risk of depression.<sup>9</sup> One factor that seems to strongly influence coping is controllability of the stressor.<sup>10</sup> When stress is perceived as uncontrollable, behavioral deficits occur, termed “learned helplessness”. In these situations, animals and people no longer attempt to cope with the stressor, even if the stressor becomes controllable.

The chronic nature of depression, especially the “kindling” effect whereby each episode of depression increases the probability of another recurrence, suggests long-term neurobiological consequences. Given that the environment influences gene expression (epigenetics) and those epigenetic changes could affect the individual’s perception of the surrounding environment, then there cannot be a strict dichotomy between genes and environment in terms of depression. Rather, there is most likely a cyclic relationship in the neuro-regulation of mood and stress responsivity, such that depression may occur because of life stress and life stress may be a result of depression.<sup>9</sup> This implies that coping with stress may break this cycle, and that complementary therapies, such as yoga, which can modify stress responses, should be helpful for depression.

## Yoga as a Treatment for Depression

Yoga is an ancient holistic health system that originated in India around 2000 BCE. In the United States today, yoga is a generally well-accepted and accessible mind-body practice focusing on physical and mental wellness. Although there is no exact definition, the word yoga is derived from Sanskrit and is often translated as “union”; this union is commonly interpreted as the unification of body, mind, and spirit to facilitate health and well-being.<sup>11-14</sup> The yoga teacher Swami Vivekananda, presenting at the Chicago Parliament of Religions in 1893, described yoga as an accessible system for health based upon the following key principles: relaxation (savasana), physical movements (asana), breathing practices (pranayama), and meditation/ positive thinking (dyhana).<sup>15</sup> Although numerous adaptations and styles of yoga have developed since 1893, these are the basic elements of yoga practice typically included in modern-day yoga classes in the United States. Recent surveys on the prevalence and practice of yoga in the United States estimate that 5–7.5% of the population has practiced yoga at some point in their lifetime; the majority of

practitioners are female, aged 34–53, and most practitioners state they use yoga for maintaining or improving physical and mental health.<sup>16–18</sup> “Hatha Yoga” is the most commonly practiced form of yoga in the United States, and is considered to be a discipline of physical, mental, and spiritual practices that are intended to provide a path towards the union of body, mind, and spirit.<sup>19,20</sup> For the purposes of this article, the term “yoga” will be used to signify Hatha yoga, in its most general form. Yoga is purportedly used by the general public for overall stress management and gentle physical exercise. Adult yoga practitioners report the most common reason for choosing yoga is for wellness/ prevention, with the secondary reason of addressing specific health conditions, particularly back and neck pain, anxiety, arthritis, depression, and fatigue.<sup>16,18</sup>

Many individuals seek complementary therapies for depression because mainstream allopathic treatments, in many instances, inadequately address the symptoms or may not address their explanatory model of depression.<sup>8,16,21–28</sup> As a common complementary therapy in the United States, yoga may be particularly helpful for depression because it can be adapted to daily mood through integrating practices to enhance physical, emotional, and spiritual health; it is easily available; and can be self-administered.<sup>16,21,29,30</sup> The slow rhythmic breathing practices and meditative/ relaxation practices of yoga are designed to induce a sense of calm, well-being, stress tolerance, and mental focus, all of which may minimize depression, anxiety, stress, and rumination.<sup>21,31–35</sup> Yoga uses gentle physical poses to enhance strength, flexibility, and balance, giving practitioners of this ancient modality a sense of control over the body.<sup>36</sup> As a form of mindful, low-impact exercise, the physical movements in yoga may have anti-depressant and anxiolytic effects.<sup>37–41</sup>

Current research supports the idea that various yoga interventions can help participants improve self-reported perceptions of stress and well-being<sup>42–47</sup> and decrease self-reported depression, dysthymia, and number of episodes of major depression.<sup>44,46,48–51</sup> Little research, however, exists on physiological or neurological mechanisms that could mediate the positive effects of yoga on mood and symptoms of psychological depression. Based on an emerging picture of how stress and mood are regulated within the nervous system, and considering the *Executive Homeostatic Network* concept that we have recently advanced,<sup>32</sup> the following sections outline potential biological mechanisms and substrates that may mediate the interactions of psychosocial stress and inborn or acquired vulnerabilities, and which could be targets for beneficial effects of yoga for stress-related disorders such as depression (Figure 1).

### Dysregulation of Stress Responses

Stress and depression are clearly linked, as stress may precipitate or exacerbate depressive symptoms and depression may be a cause and/or outcome of acute or chronic stress.<sup>25,52–54</sup> Exposure to chronic stress, whether physical or psychological in nature, has cumulative effects on the body which is referred to as “allostatic load” (AL).<sup>55</sup> Under circumstances of physical or psychological burden, the brain activates a neurobiological stress management reaction. In a short-lived situation, this reaction is adaptive and normal, designed to protect the individual from imminent threat. However, when stress is chronic, the individual’s neurobiological mechanisms become dysfunctional. Subsequently, mental and physical health can begin to deteriorate. Sometimes referred to as allostatic “overload,” permanent injury or disability may occur when the chronic stress exceeds the physical and mental capacity of the individual to cope.<sup>32,55</sup> Without availability and use of biopsychosocial resources, such as healthy coping behaviors, this can result in psychological and physical health decline leading to psychosocial functioning decline, decreased health-related quality of life, and increased incidence of comorbid conditions.<sup>9,32,56–59</sup>

Whereas activation of the sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal axis (HPAA) are essential for dealing with acute stressors, these systems can become chronically over activated given the “on-the-go” multi-tasking expectations of individuals within modern society. Ongoing arousal of the SNS/HPAA has both physical and psychological consequences: chronic stress increases the risk of gastrointestinal distress, decreases immunity (e.g., increase in colds/flu, slower wound healing), increases cardiovascular events and endocrine complications (e.g., Type 2 diabetes mellitus, erectile dysfunction, and libido issues), anxiety, and depression.<sup>60</sup> Similarly, acute symptoms of SNS/HPAA activation, such as increased heart rate and sweating, may be interpreted by the limbic system (a circuit of interconnected brain regions that process information pertaining to stress, emotion, and memory), as evidence of impending threat. This can trigger additional stress reactions, even if the individual is able to appraise that no physical or psychological cause exists for the vicious cycle. Some individuals may develop a lower threshold for the impact of a stressful situation, which may lead to the recurrence of depression.<sup>7</sup> Chronic stress has been associated with decreased dopamine and serotonin levels in the brain, which could underlie the decline in enjoyment of activities (anhedonia), typical of depression.<sup>60</sup> In addition, not only can the “top-down” psychological stress of illness cause depressive symptoms, but also the “bottom-up” inflammation related to cytokine activation can enhance symptoms<sup>32,61</sup> (as discussed below). Note also that there are significant correlations between physical and mental consequences, whereby chronic disease exacerbates mental illness and vice versa.<sup>56</sup>

Environmental psychosocial vulnerabilities influencing allostatic load include socioeconomic status, cultural definitions of health and illness, social support, and the general social environment. Individual psychosocial vulnerabilities and stressors involved may be lifestyle choices, early childhood development, personal experiences and responses to past stressors, and subjective experiences of health and illness. A key individual factor in the effect of stress may be the degree to which an individual perceives the stress to be significant and to what degree the individual thinks she/he has control over the situation.<sup>62</sup> Individual differences in personality and coping styles in the face of stressful life situations may either increase or decrease an individual’s risk for and experience of illness. Cross-sectional and longitudinal research has provided evidence to suggest that individuals with stressful life situations because of environmental factors outside of the individuals’ control (uncontrollable stress) have higher allostatic load.<sup>59,63–66</sup>

### **Neurobiological substrates that could mediate beneficial effects of yoga for depression**

Brain imaging technologies, particularly functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), have identified multiple brain regions that may be related to depression and/or participate in stress responses based upon regional changes in blood flow and cellular metabolism.<sup>67</sup> Whereas depression is heterogeneous by nature, complicating the process of localizing neural substrates of brain-behavior interactions,<sup>67</sup> emerging evidence implicates dysfunction in a circuit including cortical areas and limbic areas that regulates mood, learning, and memory processes in patients with MDD.<sup>67,68</sup> This circuit includes constituents of the Executive Homeostatic Network, most notably components of the prefrontal cortex.<sup>32</sup> Yoga may be effective for decreasing depression and anxiety symptoms by influencing functions and interactions between these structures, as noted below.

**Prefrontal cortex (PFC)**—Research suggests that symptoms of depression may result from dysfunctional activity or asymmetry of activity between the left frontal lobe (causing decreased positive affect) and the right frontal lobe (causing emotional lability and difficulty with emotional information processing and decreased arousal).<sup>69</sup> One way of assessing

liability for depression and anxiety involves assessing asymmetry of electrical activity in the frontal lobes of the brain, using electroencephalography (EEG). An “atypical” pattern of asymmetry, characterized by greater resting activity over the right frontal lobe, is believed to represent a stable marker for propensity to anxiety and depression.<sup>70</sup> For instance, this EEG pattern is found in babies of depressed mothers, individuals with seasonal affective disorder, those scoring high on depression inventories, and patients suffering from unipolar depression who are in remission.<sup>71,72</sup> The fact that frontal asymmetry is found so consistently in depressive disorders underlines the important role of the PFC in regulating mood, stress responses, and coping. Indeed, several sub-regions of the frontal lobe have been shown to be functioning abnormally during depression, including the anterior cingulate cortex (ACC), dorsolateral prefrontal cortex (DLPFC) and ventromedial prefrontal cortex (VMPFC). The executive function of the PFC implies that it is likely to be importantly involved in self-regulating coping behaviors and, thus, this region is critical for considering the neurobiological responses to yoga.

**Anterior cingulate cortex (ACC):** The cingulate cortex is an area of “limbic cortex” medial in the brain surrounding the corpus callosum. The anterior part (ACC) is in the prefrontal area, partially overlapping with the VMPFC. The ACC consistently responds to signals related to pain stimuli and immune challenge, suggesting the ACC constitutes part of the cortical representation of a viscerosensory “danger” pathway.<sup>61,73–76</sup> Damage to the ACC produces a state of “akinetic mutism”, in which individuals are awake but indifferent to pain, thirst or hunger, and show a lack of behavioral initiative (apathy).<sup>77</sup> Symptoms of apathy occur with damage to some of the inputs to the ACC, suggesting that this network of brain regions (medial prefrontal network<sup>78</sup>) is involved in organizing motivated responses to bodily challenges, such as stress, pain, or infection.

**Dorsolateral prefrontal cortex (DLPFC):** Major functions of the DLPFC relate to goal setting, sustaining attention, and maintaining emotional state to enable accomplishment of the goals set.<sup>7,79</sup> Depression and chronic pain conditions are associated with hypoactivity in the DLPFC, as indicated by associated with diminished blood flow and decreased gray matter volume. These findings may explain why individuals with depression or dysthymia tend to have a negative emotional bias, meaning that they are more likely to process and recall negative emotions and situations.<sup>68,79</sup> Yoga practice addresses this negative bias by encouraging positive self-talk and self-acceptance. In addition, it appears that when individuals have an enhanced perception of control of a situation, there is more activation in the DLPFC, which presents a potential mechanism for yoga as a coping behavior.<sup>80</sup> Through focusing on an individual’s ability to meet the mood with a combination of self-acceptance, physical movements, easeful breathing, and relaxation, it is suggested that a yoga intervention could provide individuals with an enhanced sense of control during a stressful situation or a depressive episode. The repetitive practice of yoga over sufficient number of weeks may provide a sense of accomplishment or mastery, positively reinforcing the healthy coping activity.<sup>36</sup>

Connections between the hippocampus, ACC, and DLPFC contribute to emotion processing via the *dorsal fronto-limbic circuit*. The hippocampus is integrally related to depression given that it is highly responsive to chronic stress because of its high concentration of intracellular receptors for glucocorticoids and contributions to negative feedback regulation of HPA axis activity. Just as the hippocampus is affected in cases of chronic exposure to stress, depression appears to cause atrophy to this area as well. Altered serotonin, norepinephrine (NE), and dopamine levels lead to an inability to “turn off” the chronic stress response, which can cause neuronal damage in the hippocampus because of high levels of circulating cortisol.<sup>7</sup> The amount of hippocampal atrophy has been shown to be directly related to the number and duration of depressive episodes.<sup>7</sup> Increased amygdala activity

occurs in individuals exposed to fear-inducing stimuli and those with social anxiety and phobias.<sup>80</sup> Research on the regulation of fear-driven emotions is particularly relevant given that anxiety and depression tend to overlap. Etkin (2006) demonstrated with an fMRI study that monitoring of emotional conflict occurs in the PFC and resolution of that conflict occurs with top-down inhibition of amygdala activity and activation of the ACC.<sup>81</sup> As previously noted, the ACC appears to be involved in memory, attention, and motivation, thus helping to guide actions according to one's intentions and controlling various cognitive functions (e.g., inhibiting inappropriate responses to stressors).<sup>32,60</sup> Thus, when yoga practice is effective for stress or mood disorder, it may be acting via modulation of activity in this circuit.

**Ventromedial (or subgenual) prefrontal cortex (VMPFC):** The VMPFC seems to integrate limbic, emotion-related information and translate this into modulation of autonomic and behavioral outflow.<sup>82</sup> In particular, functional studies in humans indicate that the mPFC contributes to vagal tone in humans.<sup>83,84</sup> In addition to its role in control of autonomic function, the vmPFC plays a role in regulation of mood. Interactions between the VMPFC and the amygdala allow for emotional and physiological responses to one's appraisal of situations; this is particularly relevant in depression when individuals tend to focus on negative aspects of situations and have impaired motivation.<sup>60</sup> Neuroimaging studies have found this area to be reduced in volume and metabolism during episodes of depression, which are normalized following effective treatment.<sup>85</sup> Electrical stimulation of the area (deep brain stimulation) in depressed patients can improve symptoms.<sup>86</sup> The role of the VMPFC in both mood regulation and autonomic regulation suggests that impairments of the VMPFC may contribute to the association of depression with poor health outcomes.<sup>83,86</sup>

In addition to a role in the regulation of emotion, the VMPFC contributes to neurological aspects of coping with stress. As noted previously, a factor that seems to strongly influence coping is controllability of the stressor. Uncontrollable stress leads to behavioral and immunologic deficits. Neurological correlates of learned helplessness involve excessive release of the neurotransmitter serotonin in the dorsal raphe nucleus (DRN) of the rostral brainstem. The DRN provides most of the serotonin to the forebrain, and plays an important role in stress responses and control of mood. One of the mechanisms by which controllability protects against behavioral deficits (helplessness) involves activation of the VMPFC.<sup>10</sup> The VMPFC projects directly to inhibitory interneurons on the DRN, which, in turn, reduce serotonin release. If activation of the VMPFC is prevented, however, even controllable stress leads to helplessness. Thus, the VMPFC functions as one pivotal point where factors that affect coping with stressors can act, suggesting that interventions such as yoga, which are efficacious in mitigating behavioral effects of stress, influence this structure.

Interestingly, the VMPFC is part of a constellation of brain regions that neuroimaging studies have shown are consistently active when individuals are asked to think about themselves, experience emotion, or to empathize with other people. Further, brain injury involving the VMPFC is associated with blunted emotional responses, lack of insight and poor decision-making. Thus, the VMPFC seems to function as a nodal brain region whereby social and emotional conditions interact with information from the body, related to stress and relaxation, and is likely to contribute to mechanisms by which mind-body therapies such as yoga can influence mood, social function as well autonomic output.

Major input to the VMPFC includes projections carrying feedback from the body related to stress and viscerosensory signals. Because yoga encourages mindfulness, positive self-talk, and self-acceptance, which may help increase self-confidence and sense of self, these aspects may engage the VMPFC by encouraging a focus on body movements, the breath, and other foci.<sup>21</sup> Of note, yoga does not require individuals to ignore depressive or anxious

thoughts, but rather suggests practicing non-judgmental acceptance of these, which may help minimize those thoughts.<sup>87</sup>

### Brain Chemistry

The current allopathic “usual care” for depression includes antidepressant therapy, which is based upon the monoamine hypothesis. The monoamines are the class of neurotransmitters including catecholamines (epinephrine, NE, and dopamine) and indoleamines (serotonin). The monoamine hypothesis suggests that individuals with depression have a “chemical imbalance”, particularly an imbalance of NE or serotonin levels in the CNS.<sup>5</sup> There have not been many studies investigating the effects of yoga on brain chemistry; however, practicing the physical postures of yoga has been shown to increase levels of gamma-aminobutyric acid (GABA), a neurotransmitter in the brain that can have anti-depressant and anxiolytic effects.<sup>39,88</sup> In addition, slow breathing patterns that stimulate the vagus nerve, similar to those used in yoga, have been shown to increase levels of prolactin, dopamine, NE, and serotonin (see additional discussion below).<sup>35</sup>

### Inflammation can drive depressive symptoms

Inflammation may be an important component of the underlying mechanisms of depression.<sup>89</sup> Psychosocial stress can activate peripheral and neural inflammation, which is exaggerated in individuals with MDD.<sup>89</sup> Individuals with MDD have higher circulating levels of proinflammatory cytokines, such as IL-1, IL-6, TNF-alpha; high levels of these cytokines are associated with “sickness behaviors”, such as fatigue, cognitive dysfunction, and altered sleep.<sup>90</sup> For example, when healthy volunteers are injected with a vaccine that induces peripheral cytokine production, the volunteers report feelings of depression, fatigue, and psychomotor slowing;<sup>91</sup> symptoms mediated by the brain. Cytokines may also contribute to symptoms of irritability and insomnia, which are typical in depression, via effects believed to be mediated by the dorsal ACC.<sup>90</sup> It is currently unclear whether the inflammation that drives activation of pathways in the CNS related to depression originating in the periphery or within the brain itself, or both.<sup>92</sup> Stress-induced cytokine release occurs because of SNS and HPAA activation, whereby alpha and beta-adrenergic receptors are stimulated by catecholamines and inflammatory mediators are released. The relay of peripheral inflammation signals to the CNS through neural pathways occurs through the afferent vagus nerve.<sup>75</sup> Cytokines can also act at receptors associated with the blood-brain barrier, via an intracellular cascade that allows for communication of cytokine signals into the CNS. Symptoms of depression follow cytokine-to-brain communication, leading to the activation of neural pathways that influence the basal ganglia, which are involved in motivation and motor activities,<sup>90</sup> and other brain regions involved in the control of mood, including components of the PFC and limbic system. Cytokine signaling also stimulates the HPA axis by inducing the release of corticotrophin-releasing hormone (CRH), adrenocorticotrophic hormone (ACTH), and cortisol. Under conditions of chronic stress, the negative feedback on the HPAA following increased release of cortisol leads to cortisol resistance with reduced inhibition of the inflammatory response. In this way, chronic stress can enhance susceptibility to inflammation, and thereby lead to symptoms of depression.<sup>32,90</sup> In addition, in animal models, peripheral cytokines and immune activation can induce microglial activation and cytokine production within the brain itself. In this way, cytokines can cause oxidative stress with subsequent neuronal damage in areas of the brain related to cognition and emotions—the PFC and amygdala.<sup>90</sup> Steiner and colleagues (2008) found increased microgliosis (a marker of increased neural inflammation) in the PFC, ACC, thalamus, and hippocampus in postmortem brain tissue of patients with depression who had committed suicide, providing evidence that immune activation and inflammation could play a role in the symptoms of depression in humans as well.<sup>89,93</sup> Increases in inflammatory markers, such as CRP and IL-6, are associated with decreased parasympathetic nervous

activity.<sup>90</sup> This is reflected by decreased heart rate variability (HRV), and demonstrates the dramatic multi-system effect and potential negative sequelae of inflammation in depression.

Yoga may influence the inflammatory processes involved in depression by influence on the vagus nerve. Efferent vagal nerve fibers, via the neurotransmitter acetylcholine, exert anti-inflammatory actions.<sup>94</sup> The yoga components of slow breathing, relaxation practices, mindfulness of sensations in the body, and physical postures may influence drive on brain pathways to the limbic and cortical areas involved in mood regulation and that influence parasympathetic outflow. Indeed, slow breathing practices found in yoga have been shown to affect HRV and decrease blood pressure, presumably via enhanced efferent parasympathetic responsiveness.<sup>35</sup> Thus, because inflammation is implicated as contributing to depressive symptoms, activation of the vagal anti-inflammatory pathway could be an important mechanism by which yoga practice could decrease symptoms of depression.

### Stress, gene expression, and depression

The environment influences gene expression and may contribute to the development or progression of depression, especially with regards to acute and chronic stressors and the presence or lack of social support. Life stress, particularly in the form of adverse experiences in childhood, has been shown to increase an individual's risk of depression, especially in cases of genetic predisposition.<sup>7</sup> Early life stress can increase responsiveness of the HPA, increase CRH and NE, alter serotonin expression, and decrease hippocampal volume.<sup>95</sup> These effects can occur as a result of “developmental programming”, via epigenetic mechanisms, of genes controlling stress responses and inflammation, leading to long-term risk for behavioral and mood disorders and chronic disease.<sup>89</sup> In addition, polymorphic variations in the serotonin transporter gene, at promoter region 5-HTTLPR, have been seen in individuals with depression, but the genotype of short allele (s/s allele) does not alone predict depression. Rather, individuals with the vulnerable genotype who are maltreated and are raised in an environment without social support tend to have higher rates of depression than those who have adequate social support.<sup>96</sup> For example, a study compared 57 children removed from the home for maltreatment (e.g., extreme lack of social support) with community controls; the children with the history of maltreatment and with the s/s allele, or most vulnerable genotype, had twice the rate of depression as those children without the genetic vulnerability. These findings indicate that lack of social support may be an important factor in the development of depression.<sup>95</sup> Thus, a factor in the effectiveness of yoga for depression may be the social support provided during group classes that could enhance coping in some individuals. For some individuals, the yoga practice could become a self-reinforcing behavior with a personal and group effect on mood. These behavioral modulations from yoga may assist the individual to have a healthier physical and psychological response to stress.<sup>36,97,98</sup> This idea is supported by studies that have found increased satisfaction with social support is significantly correlated with enhanced coping and inversely correlated with degree of depression in a variety of populations.<sup>99–103</sup>

### Perspectives and conclusion

In conclusion, multiple plausible neurobiological and behavioral mechanisms likely underlie the impact of yoga on depression. MDD is a complex condition involving numerous factors and symptoms, which are strongly influenced by stress. Ultimately, the ability of an individual to respond to the chronic stressors associated with depression and to individual life stressors varies greatly depending upon diverse factors, which include inborn susceptibilities and learned coping strategies. Techniques learned in yoga may help an individual change the perception and appraisal of a stressor, altering his or her affective and physiological reactions to the situation. Although little research has reported neurobiological correlates of yoga practice specifically, recent findings from human neuroimaging studies



have enabled us to advance the idea that yoga can mitigate stress responses via both top down (e.g. via psychological reappraisal) and bottom up influence (e.g., via responses to autonomic changes such as reduced inflammation or enhanced vagal tone) on PFC subregions that can control allostatic load. Thus, mind-body therapies, such as yoga, can support pharmacological and psychological therapies by improving autonomic responses to stress and self-regulating coping behaviors.<sup>21,104–106</sup> As such, a yoga intervention should be considered to assist depressed individuals to cope with life stress and their depressive symptoms. Further rigorous research is warranted to clarify specific mechanisms of yoga effectiveness.

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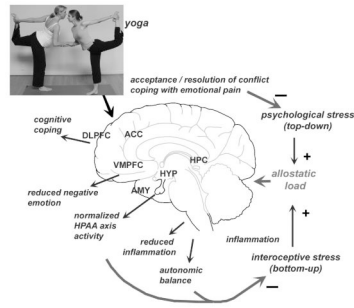
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**Figure 1.** Depiction of our model for brain substrates by which yoga may mitigate the effects of both “top-down” and “bottom-up” stress effects on allostatic load. In response to breathing and postural feedback, prefrontal cortical areas (PFC), notably VMPFC, modulate stress-responsive brain regions including the amygdala (AMY), hippocampus (HPC), and hypothalamus (HYP), to improve hypothalamic-pituitary-adrenal (HPA) axis activity, autonomic balance, and inflammation, reducing drive on bottom-up stress pathways. Meditative/mindfulness aspects of yoga encourage positive coping mediated by PFC structures including DLPFC and dorsal ACC, thereby reducing drive on top-down stress.