Brain, Behavior, & Immunity - Health 42 (2024) 100877

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx

What can the psychoneuroimmunology of yoga teach us about depression's psychopathology?

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ARTICLE INFO

Keywords:
Mind-body therapies
Treatment-resistant depression
Therapeutic yoga
Psychoneuroimmunology
Interoception
Allostatic load
BDNF
HPA axis
Stress
TRD

ABSTRACT

Depression, the most prevailing mental health condition, remains untreated in over 30% of patients. This cluster presents with sub-clinical inflammation. Investigations trialling anti-inflammatory medications had mixed results. The lack of results may result from inflammation's complexity and targeting only a few of depression's abnormal pathways. Mind-body therapies' biological and neuro-imaging studies offer valuable insights into depression psychopathology. Interestingly, mind-body therapies, like yoga, reverse the aberrant pathways in depression. These aberrant pathways include decreased cognitive function, interoception, neuroplasticity, salience and default mode networks connectivity, parasympathetic tone, increased hypothalamic-pituitary-adrenal (HPA) axis activity, and metabolic hyper/hypofunction. Abundant evidence found yogic techniques improving self-reported depressive symptoms across various populations. Yoga may be more effective in treating depression in conjunction with pharmacological and cognitive therapies. Yoga's psychoneuroimmunology teaches us that reducing allostatic load is crucial in improving depressive symptoms. Mind-body therapies promote parasympathetic tone, downregulate the HPA axis, reduce inflammation and boost immunity. The reduced inflammation promotes neuroplasticity and, subsequently, neurogenesis. Improving interoception resolves the metabolic needs prediction error and restores homeostasis. Additionally, by improving functional connectivity within the salience network, they restore the dynamic switching between the default mode and central executive networks, reducing rumination and mind-wandering. Future investigations should engineer therapies targeting the mechanisms mentioned above. The creation of multi-disciplinary health teams offering a combination of pharmacological, gene, neurofeedback, behavioural, mind-body and psychological therapies may treat treatment-resistant depression.

1. Introduction

Depression is the most prevalent mental health condition, impacting over 280 million people worldwide (IHME, 2019). Despite pharmacological advances, 30% of patients do not respond to antidepressants (Bouvier and M., 2003). Besides, chronic administration of selective serotonin reuptake inhibitor (SSRI) may have paradoxical effects such as fatigue and depleted serotonin levels (Moncrieff et al., 2022; Fava, 2020; Gray et al., 2013; Siesser et al., 2012). Current alternative treatments include psychotherapy and cognitive behavioural therapy (CBT). Despite promising results in reducing depression, stigma and limited access hinder their uptake (Sockol et al., 2011; Kim et al., 2010). Currently, apart from CBT, there are no validated regimes that can complement antidepressants long-term (Gartlehner et al., 2017).

1.1. Allostatic load and depression

Homeostasis is a dynamic physiological process promoting optional function as an organism adapts to varying external factors to survive (Mas-Bargues et al., 2023). When the system is under stress, allostasis activates to predict and respond to changing energy demands (McEwen, 2005). During allostasis, the hypothalamic-pituitary-adrenal (HPA) axis produces cortisol, and the sympathetic autonomic nervous system (ANS) releases adrenaline, increasing the metabolic rate to respond to the threat. Chronic stress damages and overloads the system, promoting inflammation and disease (McEwen, 2000). Allostatic load is the physiological cost of stress. The negative repercussions of allostatic load include reduced parasympathetic harborisation, emergence of inflammation and autoimmune conditions and chronic pain (Guidi et al., 2021).

Although depression's neurobiological mechanisms are poorly

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https://doi.org/10.1016/j.bbih.2024.100877
Received 29 November 2023; Received in revised form 11 September 2024; Accepted 28 September 2024
Available online 30 September 2024

List of abbreviations

ACC	Anterior cingulate cortex
ANS	Autonomic nervous system
BDNF	Brain-derived neurotrophic factors
CBT	Cognitive behavioural therapy
DMN	Default-mode network
GR	glucocorticoid receptors
HPA	Hypothalamic-pituitary-adrenal axis
HRV	Heart rate variability
MBTs	Mind-body Therapies
OFC	Orbitofrontal cortex
PFC	Prefrontal cortex
RCT	Randomised control trial
SNS	Sympathetic nervous system
SSRI	Selective serotonin reuptake inhibitor
TRD	Treatment-resistant depression

understood, we know stress is a risk factor (Calcia et al., 2016; Tafet and Nemeroff, 2016). The HPA axis is aberrant in treatment-resistant depression (TRD) as patients demonstrate (a) increased cortisol levels in serum and saliva, (b) reduced glucocorticoid receptors (GR) function in vitro and post-mortem enquiries (see review by Pariante and Lightman, 2008), (c) non-suppression to dexamethasone suppression test (Juruena et al., 2006), (d) increased inflammation (Anisman et al., 1999).

Studies investigating anti-inflammatory medications' efficacy in TRD found mixed results (Beckett and Niklison-Chirou ; Nettis et al., 2021; Miller and Pariante, 2020), possibly because of the multifactorial nature of inflammation and the complexity of its interactions with brain function (Turkheimer et al., 2023; Miller and Raison, 2022). Beckett and Niklison-Chirou suggest that medications such as Ketamine and Celecoxib may be particularly effective for depressed patients showcasing inflammation. Nettis et al. (2021) found minocycline only effective in patients with low-grade inflammation (CRP $\geq$3 mg/L). Husain et al. (2020) did not encounter minocycline or celecoxib to be superior to placebo in reducing bipolar depression. Importantly, depressed patients also present reduced cognitive function, interoception, parasympathetic tone, neuroplasticity, hyper/hypometabolism, salience and default mode network (DMN) connectivity (Barrett and Simmons, 2015; Avery et al., 2014; Terhaar et al., 2012; Vreeburg et al., 2009; Pariante and Lightman, 2008). The former interventions have targeted neurotransmitters and immunological aberrations using anti-inflammatory medications with limited modulation of the above mechanisms. They may have targeted only the symptoms but not the cause. Abnormal serotonin and inflammation in depression are indeed forms of allostatic load resulting from deviant metabolic function due to prediction errors of the afferent interoceptive signals (Shaffer et al., 2022; McEwen, 2000). We propose that approaches promoting top-down and bottom-up stress downregulation and brain-circuit-based interventions may produce more effective results (Scangos et al., 2023).

Mind-body therapies (MBTs), such as yoga, reduce allostatic load and improve brain-networks connectivity (Fialoke et al., 2024; Streeter et al., 2012). They may offer a non-pharmacological alternative to complement allopathic medicine. The following review explains how yoga modulates metabolic function. Due to vacuums in the literature, we had to review evidence beyond TRD.

2. Yoga

Yoga is an ancient mind-body system of lifestyle practices to improve well-being from India. Yoga is a mind-body therapy emphasising the body-mind connection in healing (Bower and Irwin, 2016). In the past 100 years, cross-pollination with Western medicine, dance, somatics, psychology and neuroscience has evolved it (Singleton, 2010). In the West, most people understand yoga solely as movement, but traditionally, yoga comprises training the mind and the breath. It includes diverse techniques encompassing movement, breathwork, relaxation, visualisation, meditation and hypnosis.

Patients experiencing neuropsychiatric conditions favour non-pharmacological therapies to improve their quality of life (Öztürk et al., 2023; Burnett-Zeigler et al., 2016; Woodward et al., 2009; Franzblau et al., 2008). Numerous studies found that patients with depression, anxiety, and trauma endorse MBTs (Love et al., 2019; Bragard et al., 2017; Niles et al., 2016).

2.1. Yoga and depression

Numerous research projects investigated the effects of yoga on depressive symptoms across different populations. Results have been mixed, although most showed that yoga significantly improved self-reported depressive symptoms (Miao et al., 2023; Bieber et al., 2021; Bringmann et al., 2022; Kinser et al., 2014). Two meta-analyses on depression reduction in Parkison (Ban et al., 2021; Jin et al., 2019) found significant improvements measured with questionnaires.

In pregnant women, eight studies found improvements in depression (Estevao, 2022; Bakri et al., 2021; Kinser et al., 2021; Duchette et al., 2021; Yuvarani et al., 2020; Battle et al., 2015; Field et al., 2013; Muzik et al., 2012) while three found no change (Uebelacker et al., 2016; Davis et al., 2015; Bershadsky et al., 2014). Yuvarani, Uebelacker, Davis, and Field found no difference in depression reduction between yoga and control. Despite all these studies being RCT, they included a small sample, heterogeneous methodology, and small effect sizes, limiting clinical translation.

2.2. Yoga as a conjunctive therapy

Evidence shows how yoga may be an effective conjunctive therapy to reduce depressive symptoms. In a qualitative study, Capon et al. (2021) identified that yoga positively complemented a CBT regime. O'Shea et al., 2022a; O'Shea et al., 2022b found therapeutic yoga in combination with group CBT more effective at reducing depressive symptoms than group CBT alone. Naveen et al. (2016) encountered that depressed patients receiving yoga or yoga and antidepressants witnessed more significant depression improvements than antidepressants alone. Sangeethalaxmi and Hankey (2023) found that adding yogic breathing to usual care in adults experiencing asthma resulted in more notable depression reduction. Nevertheless, Vollbehr et al. (2022) observed no significant changes in depressive symptoms when adding yoga to major depression's usual treatment in an RCT.

3. The psychoneuroimmunological mechanisms of yoga

Neuroimaging and biological findings suggest several interacting mechanisms behind improvements in depression from yoga. Neuroimaging studies have demonstrated structural and functional changes in brain function and connectivity, indicating yoga's potential to induce neuroplasticity (van Aalst et al., 2020; Gothe et al., 2018; Hernández et al., 2016). Biological investigations have shown that yogic practices have acute and long-term physiological effects on the nervous, immune and endocrine systems (Robinson et al., 2023; Naderi et al., 2022; Sandberg et al., 2022), with transcriptomics studies demonstrating significant changes in gene expression post-yoga, indicating that the practices induce epigenetic changes (Adhikari et al., 2022; Qu et al., 2013).

Yoga's positive outcomes may result from the synergistic effects of multiple psychoneuroimmunological mechanisms, including (a) increased interoception, (b) improved metabolism, (c) improved parasympathetic tone, (d) HPA axis downregulation, (e) reduced

inflammation and (f) augmented neuroplasticity (Fig. 1).

Although the literature contains numerous studies, small samples, lack of statistical power, and poor experimental design prevented the extraction of clinically applicable conclusions. Studies contained a heterogeneous set of methodologies that included a combination of postures, breathing and relaxation. Hence, whether the effects resulted from specific practices or are cumulative is unclear.

3.1. Interoception

Aberrant interoception is a crucial mechanism in depression, resulting in sickness behaviours (Barrett and Simmons, 2015; Raison and Miller, 2013; Harrison et al., 2009). Evidence highlights that interoceptive pathways present hypersensitivity towards aversive stimuli and reduced sensory accuracy (Avery et al., 2014; Terhaar et al., 2012; Paulus and Stein, 2010). Interoception is mediated by ascending and descending pathways to and from the insula. The insula connects with the thalamus, medial prefrontal cortex (PFC), orbitofrontal cortex (OFC) and amygdala (Lorenzetti et al., 2009; Drevets et al., 2008; Greicius et al., 2007). The insula is a critical node in the salience network, attributing affective, sensorimotor and cognitive salience to stimuli (Uddin, 2014). It modulates dynamic switching between the default mode (DMN) and the central executive networks. These areas' activity and functional connectivity are abnormal in depression. Depressed individuals have dorsolateral PFC hypoactivity, ventromedial PFC and amygdala hyperactivity (Pizzagalli and Roberts, 2021; Koenigs and Grafman, 2009; Fales et al., 2009).

Neuroimaging studies of experienced yoga practitioners found augmented interoception and insular volume, activity and connectivity (Hernández et al., 2015; Villemure et al., 2014; Farb et al., 2013). Practitioners have higher functional connectivity within the dorsal attention network (DAN), between the DAN, DMN and salience network (Santaella et al., 2019; Sevinc et al., 2018; Doll et al., 2015). Yogic techniques reduce amygdalar activity via vagal stimulation and improve insular-cortical connectivity (Gotink et al., 2018; Taren et al., 2015). Brewer et al. (2011) found cognitive control improvements and regulation of the DMN in meditators. Enhancing functional connectivity within the salience network may improve cognitive and affective depressive symptoms, such as rumination and mind-wandering, by reducing DMN activation (Chaieb et al., 2022; Hamilton et al., 2015). Meditation may be beneficial to improve salience network connectivity (Bremer et al., 2022).

3.2. Metabolism

Depressed patients display metabolic dysfunctions (Gu et al., 2021). Neuroimaging studies have found reduced blood flow and glucose metabolism in depressed patients' brains (Videbech, 2000). Corroborating transcriptomics evidence shows abnormalities in circadian patterns proteins' gene expression and mitochondria energy production (Garbett et al., 2015; Li et al., 2013).

Depression is a heterogeneous condition. Metabolic abnormalities can present with hyper or hypo activity in the Anterior Cingulate Cortex (ACC), leading to different symptoms (fatigue and agitation) (Dunlop et al., 2015). Abnormalities can be transient and manifest with temporary changes in eating, sleeping and exercise behaviours (Laposky et al., 2008; Hagobian et al., 2008; Cummings, 2006).

Depressed patients exhibit structural abnormalities in the agranular visceromotor limbic system, which is involved in interception (Barrett and Simmons, 2015). Studies found hyperactive metabolic function and structural abnormalities in the agranular visceromotor cortices (ACC, PVM PFC, POC and anterior insula) in depression's prodromal phase

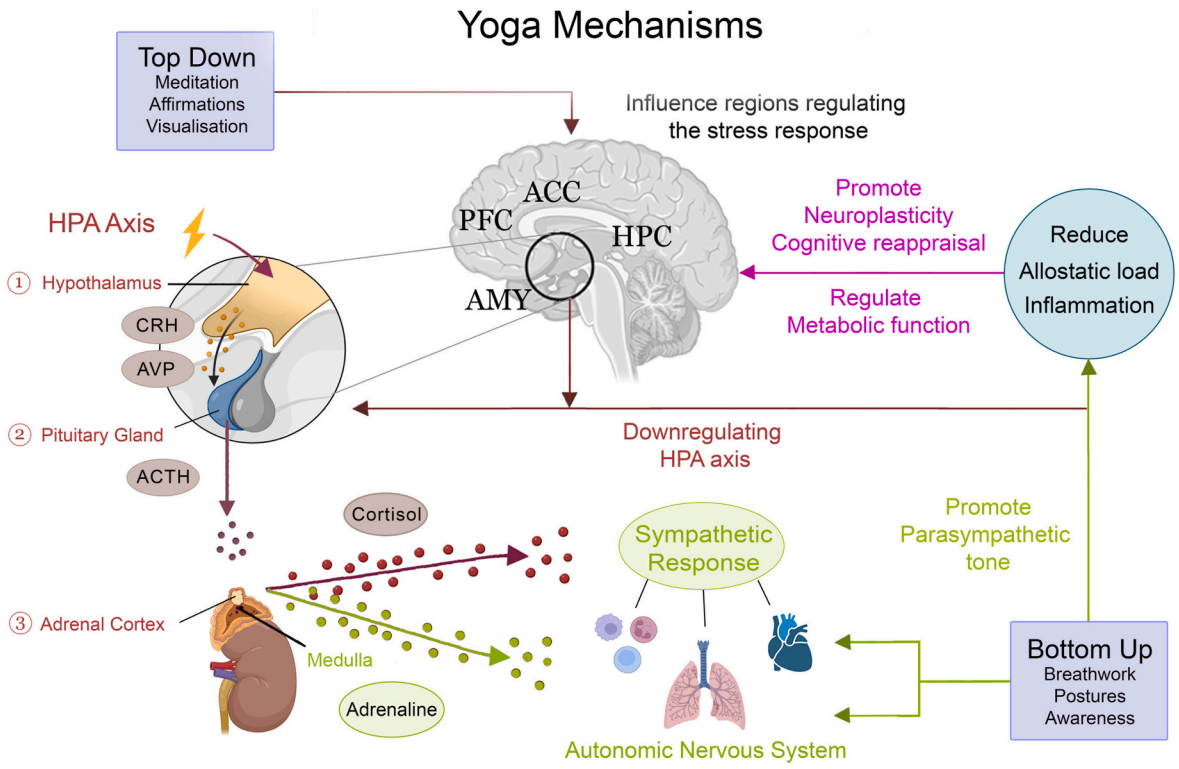

Fig. 1. Yoga Mechanisms

PFC: prefrontal cortex; ACC: anterior cingulate cortex; HPC: hippocampus; HRV: heart rate variability; AMY: amygdala. Yoga may improve depressive symptoms by downregulating the HPA axis and the sympathetic ANS. Top-down cognitive and bottom-up physiological processes mediate this downregulation, reducing overall allostatic load. Practices like meditation, positive affirmation and visualisation modulate top-down pathways. Mindful movement, interoceptive practices and breathwork modulate bottom-up pathways. Downregulating the allostatic load reduces inflammation, promotes neuroplasticity and cognitive reappraisal, and regulates metabolism.

(Lévesque et al., 2011; Boes et al., 2008). According to Barrett et al. (2016) hypothesis, depression arises because these regions compute prediction errors on the organism's metabolic needs. These regions predict interoceptive afferent signals as threats. The system responds to stressors and everyday events as if they require increasing energy, gradually depleting the resources needed to maintain long-term homeostasis (Nieuwenhuizen and Rutters, 2008). Simultaneously, the HPA axis negative feedback mechanism downregulates, leading to hypercortisolemia and the expression of pro-inflammatory cytokines (Carroll et al., 2012). These prediction errors deplete the energy reserves and produce depressive symptoms (fatigue, anhedonia), leading to reduced metabolism (Turkheimer et al., 2023). The system slows down to survive.

According to this hypothesis from Barrett et al. (2016), depression is an allostatic condition, meaning that depression results from the system's inability to find homeostasis due to prediction errors from interoceptive afferent signals. The errors result in physiological systems' failure to measure and respond to energy demands (Shaffer et al., 2022). Interoceptive processes make prediction errors on how much energy is needed. If these errors are computed for prolonged periods, they result in structural changes: atrophy in the regions modulating allostasis and increased sympathetic regions' arborisation (Capitanio and Cole, 2015; Crossley et al., 2014; Goodkind et al., 2015; Sloan et al., 2007). This sympathetic dominance increases metabolic regulation costs, resulting in long-term metabolic deficits.

Since medications and therapies do not target these mechanisms, this theory may explain the lack of results in some patients. In the prodromal phase, by teaching the brain that the world is not dangerous and does not require much energy to survive, yoga retrains the brain to lower metabolism, reducing allostatic load. Conversely, during depression, yoga restores energy reserves by promoting parasympathetic tone. Improved parasympathetic tone reduces inflammation and boosts immunity. By improving interoceptive accuracy, yoga diminishes prediction errors. Yoga either declines resource overutilisation or builds energy reserves by promoting parasympathetic tone. In other words, yoga teaches the brain how to reallocate resources and that we are safe in our bodies.

Chaya and Nagendra (2008) found yoga effective at reducing metabolism and optimising energy expenditure. This effect likely results from lessening sympathetic tone, lowering energy consumption and mobilisation. Gowri et al. (2022) encountered yoga effectively reducing BMI, FBG, PPBG, cholesterol, HOMA-IR and lipoprotein levels in diabetic patients. In a meta-analysis, Dhali et al. (2023) found yoga effective at decreasing fasting and post-prandial blood glucose and fasting insulin and insulin resistance. No studies have investigated the metabolic effect of yoga on depression. Future studies should investigate whether yoga improves brain metabolism, promotes mitochondrial gene expression and modules chemical energetic mediators such as ghrelin, leptin, and lactate (Quigley et al., 2021).

3.3. Stress downregulation

Yoga may improve depressive symptoms by downregulating the two stress response pathways, the sympathetic ANS and the HPA axis, which are hyperactive in depression (Won and Kim, 2016; Vreeburg et al., 2009). Yoga modulates stress via top-down and bottom-up mechanisms by improving the PFC's ability to regulate allostasis (Muehsam et al., 2017; Kinser et al., 2012; Taylor et al., 2010). The ANS is divided into the sympathetic and parasympathetic branches. The former is mobilised during stress to promote survival. This mode is also called fight or flight. The parasympathetic branch is activated during rest and digestion to promote healing and restoration. Both branches are essential for survival, and flexible switching between the two is a sign of stress resilience.

3.3.1. Autonomic nervous system

Numerous studies have found that yoga reduces sympathetic tone across different populations. Interventions measured physiological changes of the ANS using electrophysiological (heart rate variability - HRV) and biological markers (α-amylase). HRV is the term used to describe the variation in time intervals between consecutive heartbeats (Shaffer and Ginsberg, 2017). It reflects the autonomic nervous system's cardiovascular function regulation and is a non-invasive biomarker for assessing autonomic balance, stress response, and overall cardiovascular health. α-Amylase is an enzyme predominantly synthesised by the salivary glands and pancreas and plays a crucial role in catalysing the hydrolysis of starch into sugars in digestion (Granger et al., 2007). Salivary α-Amylase is frequently utilised as a non-invasive biomarker to assess sympathetic nervous system activity and stress-related responses.

Studies measuring HRV found yogic techniques promote parasympathetic activation via vagal toning (part of the PNS) (Žebeljan et al., 2022; Gerritsen and Band, 2018; Streeter et al., 2012; Brown and Gerbarg, 2005). Higher HRV indicates greater adaptability and stress management. Hayase and Shimada (2018) and Bhartia et al. (2019) found a significant HRV improvement in a prenatal population. While Bhartia found the HRV improvements coupled with significant stress reduction, Hayase found HRV improvements compared to the control but not significantly. Inbaraj et al. (2023) found that cancer participants receiving yoga during chemotherapy have higher HRV at the end of the intervention than usual care. In a review, Tyagi and Cohen (2016) encountered that yoga acutely improves HRV and vagal dominance. Long-term practice improves vagal tone at rest. Nevertheless, they highlight that the small sample sizes and the insufficient reporting of methods limit the ability to reach conclusions.

Studies measuring salivary α-amylase found yogic practices effective at reducing concentrations (Kukihara et al., 2022; Arrant and Stewart, 2020; Sieverdes et al., 2014; Lipschitz et al., 2013). Lower *α-a*mylase concentrations indicate reduced physiological stress and sympathetic tone (Ali and Nater, 2020). Two studies found significant α-amylase reductions in prenatal depression (Hayase and Shimada, 2018; Kusaka et al., 2016). Conversely, García-Sesnich et al. (2017) in healthy participants and Fakharirad et al. (2020) in patients post coronary artery bypass found no reductions. Nevertheless, they did find cortisol (HPA axis produced) drops. This finding indicates that *α-a*mylase may be less effective than cortisol at measuring physiological stress (Maruyama et al., 2012).

Interventions established an acute and long-term effect of yogic techniques on parasympathetic tone. While mindfulness meditation improves long-term parasympathetic tone (Wielgosz et al., 2016), breathing practices achieve this acutely (Russo et al., 2017). Balban et al. (2023) found that breathing practices extending the exhalation have the most potent effect on parasympathetic tone. Shinba et al. (2020) found that breathing and seated postures normalise autonomic activity acutely in experienced and naive participants alike.

3.3.2. HPA axis

In depression, glucocorticoid resistance and hyper/hypo cortisolemia impair the HPA axis negative feedback mechanism (Silverman and Sternberg, 2012), resulting in HPA axis abnormalities. In depression, hyperactive HPA axis modulation leads to chronic inflammation (Osimo et al., 2019; Keller et al., 2016). Depressed patients present with high concentrations of pro-inflammatory cytokines (IL-1, IL-6, TNF-alpha) and C-reactive protein (CRP) (Osimo et al., 2019; Raison and Miller, 2003). Interleukins trigger partial glucocorticoid resistance, contributing to the axis's hyperactivity (Maddock and Pariante, 2001). Enhanced inflammation results from malfunctioning glucocorticoid anti-inflammatory effects on the immune system and FKBP5's inflammation promotion (Zannas et al., 2019). FKBP5 is a gene encoding for the FKB51 protein, a negative regulator of glucocorticoid receptors (located in the brain to regulate the HPA axis down) (Malekpour et al., 2023). Chronic stress can reduce the ability of the glucocorticoid

receptors to downregulate the stress response, leading in the long-term to neuropsychiatric conditions.

Yogic interventions reduce cortisol production (Cahn et al., 2017; Matousek et al., 2011; Witek-Janusek et al., 2008; Carlson et al., 2007). Meier et al. (2021) found in saliva that yoga significantly reduces cortisol concentrations after the Trier Social Stress Test (TSST-G) compared to breathing and control. Thirthalli et al. (2013), in a 3-arm (yoga, yoga and antidepressants or antidepressants) study, found that depressed patients in the yoga groups experienced greater cortisol reductions than antidepressants alone. In the yoga-only group, depression improvements correlated with cortisol reductions.

Four studies found prenatal yoga effective at reducing cortisol concentrations in a depressed population (Chen et al., 2017; Kusaka et al., 2016; Bershadsky et al., 2014; Field et al., 2013). Chen and Bershadsky found a reduction compared to control. While Field and Kusaka found a significant cortisol reduction coupled with depression, anxiety and mood improvements prenatally, Bershadsky found a depression reduction only postnatally. Chen found higher immunoglobulin-A concentrations, suggesting that reduced cortisol may improve immunity.

3.4. Inflammation

Cytokines are small signalling proteins that cells release to regulate immune responses, inflammation, and hematopoiesis (Janeway et al., 2001). They facilitate communication between immune cells and play a crucial role in innate and adaptive immunity. Innate cytokines, such as interferons and interleukins, are quickly produced in response to infection, while adaptive cytokines, like IL-2 and IL-4, modulate longer-term, antigen-specific immune functions.

TRD presents with subclinical inflammation. Findings on yogic practices' anti and pro-inflammatory effects are inconsistent, possibly complicated by the same cytokines activating pro and anti-inflammatory pathways (Raison et al., 2018). While Cahn et al. (2017) found a decrease in IL-12 (pro-inflammatory) and an increase in IL-10 (anti-inflammatory), TNF-α, IFN-γ, IL-1β, IL-6, and IL-8 (pro-inflammatory), Bower et al. (2015) found no effect on these cytokines. Gautam et al. (2023) found a reduction in IL-17 and IL-6 (pro-inflammatory) in patients with rheumatoid arthritis, and Wahyuni et al. (2023) found a reduction in IL-6 in elderly with knee osteoarthritis compared to control. Nugent et al. (2021) found that yoga significantly reduced IL-6 but not TNF-α and CRP in severely depressed patients using antidepressants. In a review, Estevao (2022) corroborates yoga's downregulating effect on C-reactive protein and cytokines (IL-1β, IL-6, TNF-α, INF-γ).

3.5. Neuroplasticity

In depression, inflammation and high cortisol concentrations negatively affect neurogenesis, resulting in hippocampal neuronal apoptosis (Fang et al., 2023; Crochemore et al., 2005). Studies found reduced hippocampal volume and brain-derived neurotrophic factor (BDNF) gene expression in depression (Polyakova et al., 2015; Videbech and Ravnkilde, 2004).

Improved neuroplasticity may be necessary to promote hippocampal neurogenesis. Reduced HPA axis activity and increased BDNF expression induce hippocampal plasticity (Liu and Nusslock, 2018). Yogic techniques may induce neuroplasticity via improved BDNF expression (Cahn et al., 2017; Tolahunase et al., 2017; Pal et al., 2014; Gangadhar et al., 2013). Learning new motor skills may open a window of neuroplasticity, which if repeated and consolidated, results in hippocampal neurogenesis (Liu and Nusslock, 2018). Exercise increases BDNF, facilitating long-term potentiation (LTP) (Cunha et al., 2010; Rex et al., 2007). Learning new motor skills results during sleep in the new pathways' LTP. By reducing sympathetic load, the brain may experience increased CREB phosphorylation, essential in LTP (Ying et al., 2002; Abel et al., 2013). Neuroimaging studies found increased hippocampal grey matter volume in yoga and meditation practitioners (Gothe et al., 2018; Gotink et al., 2016; Hariprasad et al., 2013; Hölzel et al., 2011).

A second related mechanism promoting neuroplasticity is theta wave induction (Liu et al., 2015). These facilitate LTP in glutamatergic hippocampal neurons during sleep. During NREM sleep, hippocampal ripples induce LTP, AMPA, and NMDA receptor expression (Diekelmann and Born, 2010). This process is essential for memory consolidation and learning. In depression, sleep and memory are abnormal. Yoga induces theta waves and improves sleep quality (Azward et al., 2021; Cahn et al., 2010; Corby et al., 1978).

Nasal breathing and longer exhalation, part of breathwork practices, produce hippocampal oscillations, which are fundamental to emotional and cognitive processing (Zelano et al., 2016). Yogic practitioners have more activation in areas (superior parietal lobule, posterior cingulate gyrus, anterior supramarginal gyrus) mediating emotional regulation than controls (Wadden et al., 2018). In depression, deficits in cognitive control result in maladaptive emotional regulation strategies (Joormann and Gotlib, 2010). Yoga may improve emotional regulation by improving salience network connectivity. The increased neuroplasticity may consolidate the new emotional regulation pathways and downregulate the maladaptive ones, improving emotional arousal regulation in depression.

4. Conclusions

Yoga's psychoneuroimmunology teaches us that reducing allostatic load is crucial to improving depressive symptoms. They achieve this by promoting parasympathetic tone and downregulating the HPA axis, reducing inflammation and boosting immunity. Improved interoception reduces allostasis and enhances the insula's ability to predict energy expenditure, restoring homeostasis. Additionally, by improving functional connectivity within the salience network, yoga may restore the dynamic switching between the DMN and CEN, reducing rumination and mind-wandering. Learning can happen as inflammation diminishes and the system feels safe, promoting BDNF expression and neuroplasticity. Neurogenesis crowns the process. This model is the first to suggest that yoga's psychoneuroimmunological mechanisms result from neuroplasticity and improved metabolic function.

Antidepressants may not have worked in TRD because they treated the symptoms, not the cause. Due to expensive prediction errors in depression's prodromal phase, energy consumption skyrockets to maintain sympathetic tone and HPA axis activity. In the long term, the HPA axis becomes hyperactive due to its negative feedback mechanism downregulation, resulting in inflammation. If this scenario endures, due to exhaustion and metabolic overconsumption, the system slows down (hypometabolism) to survive, producing fatigue and anhedonia.

Further research is needed to corroborate this theory. Future investigations should a) combine neuroimaging and biological measures to assess causality and correlation; b) investigate yoga's effect on metabolism; b) be powered and include diverse populations; c) use control groups and randomisation; d) report effect sizes; d) test whether yoga in conjunction with pharmacological interventions improves depression outcomes; e) test yoga in different depression clusters; f) investigate practices' long-term effects on neuroplasticity and neurogenesis in depression g) unpack specific techniques' neurophysiology in health and disease h) run longitudinal studies assessing whether yoga promotes depression's remission and if they have long-lasting effects. These directions are vital to improving yoga's acceptability within the medical community and bringing them to the table of evidence-based care.

Yoga offers a cost-effective personalised treatment opportunity. Within prescribed protocols, practices like yoga nidra (hypnotic relaxation) offer patients a personalised space. This personal touch and care cannot be addressed (currently) with pharmacological interventions. Something as simple as bringing patients to a happy memory while in a hypnotic state, as their brains are in theta wave, can open a neuroplasticity window. This window is critical to form new pathways and

depress the maladaptive ones that lead to depression.

Evidence from psychoneuroimmunological investigations offers insights into new therapeutic targets. Possible targets include the HPA axis, parasympathetic tone, large brain circuits, insulin receptors, anti-inflammatory cytokines and neurotrophic factors. Pharmacological, gene, biofeedback, mind-body and cognitive therapies targeting these pathways must be engineered.

Allopathic healthcare providers should collaborate with complementary therapists to design holistic programs. Knowledge from both sciences should inform patient care. Establishing interdisciplinary healthcare teams may provide an effective and cost-efficient strategy to alleviate TRD. Combining and integrating multiple modalities will solve humanity's most taxing conditions.

CRediT authorship contribution statement

Carola Chiarpenello: Writing – review & editing, Supervision, Federico Turkheimer: Writing – review & editing. **Katja Brodmann:** Yannis Paloyelis: Writing – review & editing, Supervision.

Declaration of competing interest

The author declares that she has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgements

Carola Chiarpenello is supported by the British Research Council (BRC), KCL BSc Neuroscience and Psychology Programme and Prof Carmine Pariante's SPI Lab. Dr Katja Brodmann, Dr Yannis Paloyelis and Prof Federico Turkheimer gave editing feedback.

References

Abel, T., Havekes, R., Saletin, J.M., Walker, M.P., 2013. Sleep, plasticity and memory from molecules to whole-brain networks. Curr. Biol. 23. https://doi.org/10.1016/J.CUB.2013.07.025.

Adhikari, B., Starkweather, A., Xu, W., Acabchuk, R.L., Ramesh, D., Eze, B., Yang, Y., Yang, G.S., Walker, J., Laubenbacher, R., Park, C.L., 2022. A feasibility study on yoga's mechanism of action for chronic low back pain: psychological and neurophysiological changes, including global gene expression and DNA methylation, following a yoga intervention for chronic low back pain. Pilot. Feasibility Stud. 8, 1–16. https://doi.org/10.1186/S40814-022-01103-2/TABLES/2.

Ali, N., Nater, U.M., 2020. Salivary alpha-amylase as a biomarker of stress in behavioral medicine. Int. J. Behav. Med. 27, 337–342. https://doi.org/10.1007/S12529-019-09843-X/METRICS.

Anisman, H., Ravindran, A.V., Griffiths, J., Merali, Z., 1999. Endocrine and cytokine correlates of major depression and dysthymia with typical or atypical features. Mol. Psychiatr. 4 (2 4), 182–188. https://doi.org/10.1038/sj.mp.4000436, 1999.

Arrant, K., Stewart, M., 2020. The effects of a yoga intervention. J. Interprofes. Pract. Collab. 2.

Avery, J.A., Drevets, W.C., Moseman, S.E., Bodurka, J., Barcalow, J.C., Simmons, W.K., 2014. Major depressive disorder is associated with abnormal interoceptive activity and functional connectivity in the insula. Biol. Psychiatr. 76, 258–266. https://doi.org/10.1016/j.biopsych.2013.11.027.

Azward, H., Ramadhany, S., Pelupessy, N., Usman, A.N., Bara, F.T., 2021. Prenatal yoga exercise improves sleep quality in the third trimester of pregnant women. Gac. Sanit. 35, S258–S262. https://doi.org/10.1016/J.GACETA.2021.10.030.

Bakri, K.R.R., Usman, A.N., Syamsuddin, S., Idris, I., Limoa, E., 2021. The effectiveness of gentle prenatal yoga on the recovery of depression level in pregnant women aged. Gac. Sanit. 35, S310–S313. https://doi.org/10.1016/J.GACETA.2021.10.042.

Balban, M.Y., Neri, E., Kogon, M.M., Weed, L., Nouriani, B., Jo, B., Holl, G., Zeitzer, J.M., Spiegel, D., Huberman, A.D., 2023. Brief structured respiration practices enhance mood and reduce physiological arousal. Cell Rep. Med. 4, 100895. https://doi.org/10.1016/J.XCRM.2022.100895.

Ban, M., Yue, X., Dou, P., Zhang, P., 2021. The effects of yoga on patients with Parkinson's disease: a meta-analysis of randomized controlled trials. Behav. Neurol. 2021. https://doi.org/10.1155/2021/5582488.

Barrett, L.F., Simmons, W.K., 2015. Interoceptive predictions in the brain. Nat. Rev. Neurosci. 16 (7 16), 419–429. https://doi.org/10.1038/nrn3950, 2015.

Barrett, L.F., Quigley, K.S., Hamilton, P., 2016. An active inference theory of allostasis and interoception in depression. Phil. Trans. Biol. Sci. 371. https://doi.org/10.1098/RSTB.2016.0011.

Battle, C.L., Uebelacker, L.A., Magee, S.R., Sutton, K.A., Miller, I.W., 2015. Potential for prenatal yoga to serve as an intervention to treat depression during pregnancy. Wom. Health Issues 25 (2), 134–141. https://doi.org/10.1016/j.whi.2014.12.003.

Beckett, C.W., Niklison-Chirou, M.V., n.d. PERSPECTIVE The role of immunomodulators in treatment-resistant depression: case studies. https://doi.org/10.1038/s41420-022-01147-6.

Bershadsky, S., Trumpfheller, L., Kimble, H.B., Pipaloff, D., Yim, I.S., 2014. The effect of prenatal Hatha yoga on affect, cortisol and depressive symptoms. Compl. Ther. Clin. Pract. 20, 106–113. https://doi.org/10.1016/J.CTCP.2014.01.002.

Bhartia, N., Shankar, N., Rajaram, S., Gupta, M., 2019. Effects of Antenatal Yoga on Maternal Stress and Clinical Outcomes in North Indian Women: A Randomised Controlled Trial.

Bieber, M., Görgülü, E., Schmidt, D., Zabel, K., Etyemez, S., Friedrichs, B., Prvulovic, D., Reif, A., Oertel, V., 2021. Effects of body-oriented yoga: a RCT study for patients with major depressive disorder. Eur. Arch. Psychiatr. Clin. Neurosci. 271, 1217–1229. https://doi.org/10.1007/S00406-021-01277-5/TABLES/3.

Boes, A.D., McCormick, L.M., Coryell, W.H., Nopoulos, P., 2008. Rostral anterior cingulate cortex volume correlates with depressed mood in normal healthy children. Biol. Psychiatr. 63, 391–397. https://doi.org/10.1016/j.biopsych.2007.07.018.

Bouvier, N.T.T., M, H., 2003. Development of antidepressant drugs. Experience and prospects. Presse Med. 32, 519–522.

Bower, J.E., Irwin, M.R., 2016. Mind–body therapies and control of inflammatory biology: a descriptive review. Brain Behav. Immun. 51, 1–11. https://doi.org/10.1016/J.BBI.2015.06.012.

Bower, J.E., Crosswell, A.D., Stanton, A.L., Crespi, C.M., Winston, D., Arevalo, J., Ma, J., Cole, S.W., Ganz, P.A., 2015. Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. Cancer 121, 1231–1240. https://doi.org/10.1002/CNCR.29194.

Bragard, I., Etienne, A.M., Faymonville, M.E., Coucke, P., Lifrange, E., Schroeder, H., Wagener, A., Dupuis, G., Jerusalem, G., 2017. Une étude comparative non randomisée de l'utilisation de l'autohypnose, du yoga et de la thérapie cognitivo-comportementale visant à réduire la détresse émotionnelle chez des patientes atteintes du cancer du sein. IJCEH (Int. J. Clin. Exp. Hypn.) 65, 189–209. https://doi.org/10.1080/00207144.2017.1276363.

Bremer, B., Wu, Q., Mora Alvarez, M.G., Holzel, B.K., Wilhelm, M., Hell, E., Tavacioglu, E.E., Torske, A., Koch, K., 2022. Mindfulness meditation increases default mode, salience, and central executive network connectivity. Sci. Rep. 12 (1), 13219. https://doi.org/10.1038/s41598-022-17325-6.

Brewer, J.A., Worhunsky, P.D., Gray, J.R., Tang, Y.Y., Weber, J., Kober, H., 2011. Meditation experience is associated with differences in default mode network activity and connectivity. Proc. Natl. Acad. Sci. U. S. A. 108, 20254–20259. https://doi.org/10.1073/PNAS.1112029108/SUPPL_FILE/SFIG01.PDF.

Bringmann, H.C., Michalsen, A., Jeitler, M., Kessler, C.S., Brinkhaus, B., Brunnhuber, S., Sedlmeier, P., 2022. Meditation-based lifestyle modification in mild to moderate depression—a randomized controlled trial. Depress. Anxiety 39, 363–375. https://doi.org/10.1002/DA.23249.

Brown, R.P., Gerbarg, P.L., 2005. Sudarshan Kriya yogic breathing in the treatment of stress, anxiety, and depression: Part I - neurophysiologic model. J. Alternative Compl. Med. 11, 189–201. https://doi.org/10.1089/ACM.2005.11.189.

Burnett-Zeigler, I., Schuette, S., Victorson, D., Wisner, K.L., 2016. Mind–body approaches to treating mental health symptoms among disadvantaged populations: a comprehensive review. J. Alternative Compl. Med. 22, 115. https://doi.org/10.1089/ACM.2015.0038.

Cahn, B.R., Delorme, A., Polich, J., 2010. Occipital gamma activation during Vipassana meditation. Cognit. Process. 11, 39–56. https://doi.org/10.1007/S10339-009-0352-1/FIGURES/7.

Cahn, B.R., Goodman, M.S., Peterson, C.T., Maturi, R., Mills, P.J., 2017. Yoga, meditation and mind-body health: increased BDNF, cortisol awakening response, and altered inflammatory marker expression after a 3-month yoga and meditation retreat. Front. Hum. Neurosci. 11, 229690. https://doi.org/10.3389/FNHUM.2017.00315/BIBTEX.

Calcia, M.A., Bonsall, D.R., Bloomfield, P.S., Selvaraj, S., Barichello, T., Howes, O.D., 2016. Stress and neuroinflammation: a systematic review of the effects of stress on microglia and the implications for mental illness. Psychopharmacology. https://doi.org/10.1007/s00213-016-4218-9.

Capitanio, J.P., Cole, S.W., 2015. Social instability and immunity in rhesus monkeys: the role of the sympathetic nervous system. Phil. Trans. Biol. Sci. 370, 20140104. https://doi.org/10.1098/RSTB.2014.0104.

Capon, H., O'Shea, M., Evans, S., McIver, S., 2021. Yoga complements cognitive behaviour therapy as an adjunct treatment for anxiety and depression: qualitative findings from a mixed-methods study. Psychol. Psych. 94, 1015–1035. https://doi.org/10.1111/PAPT.12343.

Carlson, L.E., Speca, M., Faris, P., Patel, K.D., 2007. One year pre–post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain Behav. Immun. 21, 1038–1049. https://doi.org/10.1016/J.BBI.2007.04.002.

Carroll, B.J., Iranmanesh, A., Keenan, D.M., Cassidy, F., Wilson, W.H., Veldhuis, J.D., 2012. Pathophysiology of hypercortisolism in depression: pituitary and adrenal responses to low glucocorticoid feedback. Acta Psychiatr. Scand. 125, 478. https://doi.org/10.1111/J.1600-0447.2011.01821.X.

Chaieb, L., Hoppe, C., Fell, J., 2022. Mind wandering and depression: a status report. Neurosci. Biobehav. Rev. 133, 104505. https://doi.org/10.1016/J.NEUBIOREV.2021.12.028.

Chaya, M.S., Nagendra, H.R., 2008. Long-term effect of yogic practices on diurnal metabolic rates of healthy subjects. Int. J. Yoga 1, 27. https://doi.org/10.4103/0973-6131.36761.

Chen, P.J., Yang, L., Chou, C.C., Li, C.C., Chang, Y.C., Liaw, J.J., 2017. Effects of prenatal yoga on women's stress and immune function across pregnancy: a randomized controlled trial. Compl. Ther. Med. 31, 109–117. https://doi.org/10.1016/j.ctim.2017.03.003.

Corby, J.C., Roth, W.T., Zarcone, V.P., Kopell, B.S., 1978. Psychophysiological correlates of the practice of tantric yoga meditation. Arch. Gen. Psychiatr. 35, 571–577. https://doi.org/10.1001/ARCHPSYC.1978.01770290053005.

Crochemore, C., Lu, J., Wu, Y., Liposits, Z., Sousa, N., Holsboer, F., Almeida, O.F.X., 2005. Direct targeting of hippocampal neurons for apoptosis by glucocorticoids is reversible by mineralocorticoid receptor activation. Mol. Psychiatr. 10 (8 10), 790–798. https://doi.org/10.1038/sj.mp.4001679, 2005.

Crossley, N.A., Mechelli, A., Scott, J., Carletti, F., Fox, P.T., Mcguire, P., Bullmore, E.T., 2014. The hubs of the human connectome are generally implicated in the anatomy of brain disorders. Brain 137, 2382–2395. https://doi.org/10.1093/BRAIN/AWU132.

Cummings, D.E., 2006. Ghrelin and the short- and long-term regulation of appetite and body weight. Physiol. Behav. 89, 71–84. https://doi.org/10.1016/J.PHYSBEH.2006.05.022.

Cunha, C., Brambilla, R., Thomas, K.L., 2010. A simple role for BDNF in learning and memory? Front. Mol. Neurosci. 3, 865. https://doi.org/10.3389/NEURO.02.001.2010/BIBTEX.

Davis, K., Goodman, S.H., Leiferman, J., Taylor, M., Dimidjian, S., 2015. A randomized controlled trial of yoga for pregnant women with symptoms of depression and anxiety. Compl. Ther. Clin. Pract. 21, 166–172. https://doi.org/10.1016/J.CTCP.2015.06.005.

Dhali, B., Chatterjee, S., Das, S.S., Cruz, M.D., 2023. Effect of yoga on insulin resistance in type 2 diabetes: a systematic review and meta-analysis. Clin. Diabetol. 12, 201–208. https://doi.org/10.5603/DK.A2023.0022.

Diekelmann, S., Born, J., 2010. The memory function of sleep. Nat. Rev. Neurosci. 11 (2 11), 114–126. https://doi.org/10.1038/nrn2762, 2010.

Doll, A., Hölzel, B.K., Boucard, C.C., Wohlschläger, A.M., Sorg, C., 2015. Mindfulness is associated with intrinsic functional connectivity between default mode and salience networks. Front. Hum. Neurosci. 9, 134814. https://doi.org/10.3389/FNHUM.2015.00461/BIBTEX.

Drevets, W.C., Price, J.L., Furey, M.L., 2008. Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. Brain Struct. Funct. 213 (1 213), 93–118. https://doi.org/10.1007/S00429-008-0189-X, 2008.

Duchette, C., Tolusso, D.V., Stone, W.J., Blankenship, M.M., Tinius, R.A., 2021. Prenatal yoga and mental health during the COVID-19 pandemic: a randomized-control trial. OBM Integra. Comple.Med. 6 (051 6), 1–17. https://doi.org/10.21926/OBM.ICM.2104051, 2021.

Dunlop, B.W., Kelley, M.E., McGrath, C.L., Craighead, W.E., Mayberg, H.S., 2015. Preliminary findings supporting insula metabolic activity as a predictor of outcome to psychotherapy and medication treatments for depression. J. Neuropsychiatry Clin. Neurosci. 27, 237–239. https://doi.org/10.1176/APPI.NEUROPSYCH.14030048/ASSET/IMAGES/LARGE/APPI.NEUROPSYCH.14030048F1.JPEG.

Estevao, C., 2022. The role of yoga in inflammatory markers. Brain Behav. Immun. Health 20, 100421. https://doi.org/10.1016/J.BBIH.2022.100421.

Fakharirad, F., Ghazalian, F., Nikbakht, H., Lotfian, S., Nikpajouh, A., 2020. The effect of 8 weeks of combined yoga and rehabilitation training on salivary levels of alpha-amylase and cortisol in patients after coronary artery bypass grafting. Res. Cardiovasc. Med. 9, 16. https://doi.org/10.4103/RCM.RCM_4_20.

Fales, C.L., Barch, D.M., Rundle, M.M., Mintun, M.A., Mathews, J., Snyder, A.Z., Sheline, Y.I., 2009. Antidepressant treatment normalizes hypoactivity in dorsolateral prefrontal cortex during emotional interference processing in major depression. J. Affect. Disord. 112, 206–211. https://doi.org/10.1016/J.JAD.2008.04.027.

Fang, S., Wu, Z., Guo, Y., Zhu, W., Wan, C., Yuan, N., Chen, Jianbei, Hao, W., Mo, X., Guo, X., Fan, L., Li, X., Chen, Jiaxu, 2023. Roles of microglia in adult hippocampal neurogenesis in depression and their therapeutics. Front. Immunol. 14, 1193053. https://doi.org/10.3389/FIMMU.2023.1193053/BIBTEX.

Farb, N.A.S., Segal, Z.V., Anderson, A.K., 2013. Mindfulness meditation training alters cortical representations of interoceptive attention. Soc. Cognit. Affect Neurosci. 8, 15–26. https://doi.org/10.1093/SCAN/NSS066.

Fava, G.A., 2020. Antidepressant drugs worsen the conditions they are supposed to treat? The clinical foundations of the oppositional model of tolerance. Ther. Adv. Psychopharm. 10, 204512532097032. https://doi.org/10.1177/2045125320970325.

Fialoke, S., Tripathi, V., Thakral, S., Dhawan, A., Majahan, V., Garg, R., 2024. Functional connectivity changes in meditators and novices during yoga nidra practice. Sci. Rep. 14 (1), 12957. https://doi.org/10.1038/s41598-024-63765-7.

Field, T., Diego, M., Delgado, J., Medina, L., 2013. Yoga and social support reduce prenatal depression, anxiety and cortisol. J. Bodyw. Mov. Ther. 17, 397–403. https://doi.org/10.1016/j.jbmt.2013.03.010.

Franzblau, S.H., Echevarria, S., Smith, M., Van Cantfort, T.E., 2008. A preliminary investigation of the effects of giving testimony and learning yogic breathing techniques on battered women's feelings of depression, 23, 1800–1808. https://doi.org/10.1177/0886260508314329.

Gangadhar, B.N., Naveen, G.H., Rao, M.G., Thirthalli, J., Varambally, S., 2013. Positive antidepressant effects of generic yoga in depressive out-patients: a comparative study. Indian J. Psychiatr. 55. https://doi.org/10.4103/0019-5545.116312.

Garbett, K.A., Vereczkei, A., Kálmán, S., Wang, L., Korade, Z., Shelton, R.C., Mirnics, K., 2015. Fibroblasts from patients with major depressive disorder show distinct transcriptional response to metabolic stressors. Transl. Psychiatry 5 (3 5). https://doi.org/10.1038/tp.2015.14, 2015 e523–e523.

García-Sesnich, J.N., Flores, M.G., Ríos, M.H., Aravena, J.G., 2017. Longitudinal and immediate effect of kundalini yoga on salivary levels of cortisol and activity of alpha-amylase and its effect on perceived stress. Int. J. Yoga 10, 73. https://doi.org/10.4103/IJOY.IJOY_45_16.

Gartlehner, G., Wagner, G., Matyas, N., Titscher, V., Greimel, J., Lux, L., Gaynes, B.N., Viswanathan, M., Patel, S., Lohr, K.N., 2017. Pharmacological and non-pharmacological treatments for major depressive disorder: review of systematic reviews. BMJ Open 7 (6), e014912. https://doi.org/10.1136/bmjopen-2016-014912.

Gautam, S., Kumar, R., Kumar, U., Kumar, S., Luthra, K., Dada, R., 2023. Yoga maintains Th17/Treg cell homeostasis and reduces the rate of T cell aging in rheumatoid arthritis: a randomized controlled trial. Sci. Rep. 13 (1 13), 1–13. https://doi.org/10.1038/s41598-023-42231-w, 2023.

Gerritsen, R.J.S., Band, G.P.H., 2018. Breath of life: the respiratory vagal stimulation model of contemplative activity. Front. Hum. Neurosci. 12, 393151. https://doi.org/10.3389/FNHUM.2018.00397/BIBTEX.

Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., Ortega, B.N., Zaiko, Y.V., Roach, E.L., Korgaonkar, M.S., Grieve, S.M., Galatzer-Levy, I., Fox, P.T., Etkin, A., 2015. Identification of a common neurobiological substrate for mental illness. JAMA Psychiatr. 72, 305–315. https://doi.org/10.1001/JAMAPSYCHIATRY.2014.2206.

Gothe, N.P., Hayes, J.M., Temali, C., Damoiseaux, J.S., 2018. Differences in brain structure and function among yoga practitioners and controls. Front. Integr. Neurosci. 12, 349899. https://doi.org/10.3389/FNINT.2018.00026/BIBTEX.

Gotink, R.A., Meijboom, R., Vernooij, M.W., Smits, M., Hunink, M.G.M., 2016. 8-week Mindfulness Based Stress Reduction induces brain changes similar to traditional long-term meditation practice – a systematic review. Brain Cognit. 108, 32–41. https://doi.org/10.1016/J.BANDC.2016.07.001.

Gotink, R.A., Vernooij, M.W., Ikram, M.A., Niessen, W.J., Krestin, G.P., Hofman, A., Tiemeier, H., Hunink, M.G.M., 2018. Meditation and yoga practice are associated with smaller right amygdala volume: the Rotterdam study. Brain Imaging Behav. 12, 1631–1639. https://doi.org/10.1007/S11682-018-9826-Z/TABLES/4.

Gowri, M.M., Rajendran, J., Srinivasan, A.R., Bhavanani, A.B., Meena, R., 2022. Impact of an integrated yoga therapy protocol on insulin resistance and glycemic control in patients with type 2 diabetes mellitus. Rambam Maimon. Med. J. 13, 5. https://doi.org/10.5041/RMMJ.10462.

Granger, D.A., Kivlighan, K.T., el-Sheikh, M., Gordis, E.B., Stroud, L.R., 2007. Salivary alpha-amylase in biobehavioral research: recent developments and applications. Ann. N. Y. Acad. Sci. 1098, 122–144. https://doi.org/10.1196/annals.1384.008.

Gray, N.A., Milak, M.S., Delorenzo, C., Ogden, R.T., Huang, Y.Y., Mann, J.J., Parsey, R. V., 2013. Antidepressant treatment reduces serotonin-1A autoreceptor binding in major depressive disorder. Biol. Psychiatr. 74, 26–31. https://doi.org/10.1016/j.biopsych.2012.11.012.

Greicius, M.D., Flores, B.H., Menon, V., Glover, G.H., Solvason, H.B., Kenna, H., Reiss, A. L., Schatzberg, A.F., 2007. Resting-state functional connectivity in major depression: abnormally increased contributions from subgenual cingulate cortex and thalamus. Biol. Psychiatr. 62, 429–437. https://doi.org/10.1016/j.biopsych.2006.09.020.

Gu, X., Ke, S., Wang, Q., Zhuang, T., Xia, C., Xu, Y., Yang, L., Zhou, M., 2021. Energy metabolism in major depressive disorder: recent advances from omics technologies and imaging. Biomed. Pharmacother. 141, 111869. https://doi.org/10.1016/J.BIOPHA.2021.111869.

Guidi, J., Lucente, M., Sonino, N., Fava, G.A., 2021. Allostatic load and its impact on health: a systematic review. Psychother. Psychosom. 90 (1), 11–27. https://doi.org/10.1159/000510696.

Hagobian, T.A., Sharoff, C.G., Braun, B., 2008. Effects of short-term exercise and energy surplus on hormones related to regulation of energy balance. Metabolism 57, 393–398. https://doi.org/10.1016/J.METABOL.2007.10.016.

Hamilton, J.P., Farmer, M., Fogelman, P., Gotlib, I.H., 2015. Depressive rumination, the default-mode network, and the dark matter of clinical neuroscience. Biol. Psychiatr. 78, 224–230. https://doi.org/10.1016/j.biopsych.2015.02.020.

Hariprasad, V.R., Varambally, S., Shivakumar, V., Kalmady, S.V., Venkatasubramanian, G., Gangadhar, B.N., 2013. Yoga increases the volume of the hippocampus in elderly subjects. Indian J. Psychiatr. 55. https://doi.org/10.4103/0019-5545.116309.

Harrison, N.A., Brydon, L., Walker, C., Gray, M.A., Steptoe, A., Dolan, R.J., Critchley, H. D., 2009. Neural origins of human sickness in interoceptive responses to inflammation. Biol. Psychiatr. 66, 415–422. https://doi.org/10.1016/j.biopsych.2009.03.007.

Hayase, M., Shimada, M., 2018. Effects of maternity yoga on the autonomic nervous system during pregnancy. J. Obstet. Gynaecol. Res. 44, 1887–1895. https://doi.org/10.1111/JOG.13729.

Hernández, S.E., Suero, J., Rubia, K., González-Mora, J.L., 2015. Monitoring the neural activity of the state of mental silence while practicing sahaja yoga meditation. J. Alternative Compl. Med. 21, 175–179. https://doi.org/10.1089/ACM.2013.0450/FORMAT/EPUB.

Hernández, S.E., Suero, J., Barros, A., González-Mora, J.L., Rubia, K., 2016. Increased grey matter associated with long-term sahaja yoga meditation: a voxel-based morphometry study. PLoS One 11, e0150757. https://doi.org/10.1371/JOURNAL.PONE.0150757.

Hölzel, B.K., Carmody, J., Vangel, M., Congleton, C., Yerramsetti, S.M., Gard, T., Lazar, S. W., 2011. Mindfulness practice leads to increases in regional brain gray matter

density. Psychiatry Res. Neuroimaging. 191, 36–43. https://doi.org/10.1016/J.PSCYCHRESNS.2010.08.006.
Husain, M.I., Chaudhry, I.B., Khoso, A.B., Husain, M.O., Hodsoll, J., Ansari, M.A., Naqvi, H.A., Minhas, F.A., Carvalho, A.F., Meyer, J.H., Deakin, B., Mulsant, B.H., Husain, N., Young, A.H., 2020. Minocycline and celecoxib as adjunctive treatments for bipolar depression: a multicentre, factorial design randomised controlled trial. Lancet Psychiatr. 7 (6), 515–527. https://doi.org/10.1016/S2215-0366(20)30138-3.
IHME, 2019. Global burden of disease (GBD) study [WWW Document]. URL11.13.23. https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2019-permalink/d780dffbe8a381b25e1416884959e88b.
Inbaraj, G., Udupa, K., Raghavendra, R.M., Ram, A., Patil, S., Rajeswaran, J., Nandakumar, K.K., Belur, S., Arjun, K., Govindaraj, R., Bayari, S.K., Sathyaprabha, T. N., 2023. Effects of an 18-week integrated yoga program on cardiac autonomic function in breast cancer patients undergoing adjuvant chemotherapy: a randomized controlled trial. Integr. Cancer Ther. 22. https://doi.org/10.1177/15347354231168795.
Janeway, CA Jr, Travers, P., Walport, M., 2001. Immunobiology: the immune system in health and disease. Garland Science. https://www.ncbi.nlm.nih.gov/books/NBK10775/.
Jin, X., Wang, L., Liu, S., Zhu, L., Loprinzi, P.D., Fan, X., 2019. The impact of mind-body exercises on motor function, depressive symptoms, and quality of life in Parkinson's disease: a systematic review and meta-analysis. Int. J. Environ. Res. Publ. Health 17, 31. https://doi.org/10.3390/IJERPH17010031, 17, 31. 2020.
Joormann, J., Gotlib, I.H., 2010. Emotion regulation in depression: relation to cognitive inhibition. Cognit. Emot. 24, 281. https://doi.org/10.1080/02699930903407948.
Juruena, M.F., Cleare, A.J., Papadopoulos, A.S., Poon, L., Lightman, S., Pariante, C.M., 2006. Different responses to dexamethasone and prednisolone in the same depressed patients. Psychopharmacology (Berl) 189, 225–235. https://doi.org/10.1007/S00213-006-0555-4/TABLES/1.
Keller, J., Gomez, R., Williams, G., Lembke, A., Lazzeroni, L., Murphy, G.M., Schatzberg, A.F., 2016. HPA axis in major depression: cortisol, clinical symptomatology and genetic variation predict cognition. Mol. Psychiatr. 22 (4 22), 527–536. https://doi.org/10.1038/mp.2016.120, 2016.
Kim, J., La Porte, L.M., Corcoran, M., Magasi, S., Batza, J., Silver, R.K., 2010. Barriers to mental health treatment among obstetric patients at risk for depression. YMOB 202, 312.e1–312.e5. https://doi.org/10.1016/j.ajog.2010.01.004.
Kinser, P.A., Goehler, L.E., Taylor, A.G., 2012. How might yoga help depression? A neurobiological perspective. Explore 8, 118–126. https://doi.org/10.1016/J.EXPLORE.2011.12.005.
Kinser, P.A., Elswick, R.K., Kornstein, S., 2014. Potential long-term effects of a mind-body intervention for women with major depressive disorder: sustained mental health improvements with a pilot yoga intervention. Arch. Psychiatr. Nurs. 28, 377–383. https://doi.org/10.1016/J.APNU.2014.08.014.
Kinser, P.A., Thacker, L.R., Rider, A., Moyer, S., Amstadter, A.B., Mazzeo, S.E., Bodnar-Deren, S., Starkweather, A., 2021. Feasibility, acceptability, and preliminary effects of "mindful moms": a mindful physical activity intervention for pregnant women with depression. Nurs. Res. 70, 95–105. https://doi.org/10.1097/NNR.0000000000000485.
Koenigs, M., Grafman, J., 2009. The functional neuroanatomy of depression: distinct roles for ventromedial and dorsolateral prefrontal cortex. Behav. Brain Res. 201, 239–243. https://doi.org/10.1016/J.BBR.2009.03.004.
Kukihara, H., Ando, M., Yamawaki, N., 2022. The effects of yoga and mindful meditation on elderly care worker's burnout: a CONSORT-compliant randomized controlled trial. J. Rural Med. 17, 14–20. https://doi.org/10.2185/JRM.2021-021.
Kusaka, M., Matsuzaki, M., Shiraishi, M., Haruna, M., 2016. Immediate stress reduction effects of yoga during pregnancy: one group pre–post test. Women Birth 29, e82–e88. https://doi.org/10.1016/J.WOMBI.2016.04.003.
Laposky, A.D., Bass, J., Kohsaka, A., Turek, F.W., 2008. Sleep and circadian rhythms: key components in the regulation of energy metabolism. FEBS Lett. 582, 142–151. https://doi.org/10.1016/J.FEBSLET.2007.06.079.
Lévesque, M.L., Beauregard, M., Ottenhof, K.W., Fortier, É., Tremblay, R.E., Brendgen, M., Pérusse, D., Dionne, G., Robaey, P., Vitaro, F., Boivin, M., Booij, L., 2011. Altered patterns of brain activity during transient sadness in children at familial risk for major depression. J. Affect. Disord. 135, 410–413. https://doi.org/10.1016/J.JAD.2011.08.010.
Li, J.Z., Bunney, B.G., Meng, F., Hagenauer, M.H., Walsh, D.M., Vawter, M.P., Evans, S.J., Choudary, P.V., Cartagena, P., Barchas, J.D., Schatzberg, A.F., Jones, E.G., Myers, R. M., Watson, S.J., Akil, H., Bunney, W.E., 2013. Circadian patterns of gene expression in the human brain and disruption in major depressive disorder. Proc. Natl. Acad. Sci. U. S. A. 110, 9950–9955. https://doi.org/10.1073/PNAS.1305814110/SUPPL_FILE/PNAS.201305814SI.PDF.
Lipschitz, D.L., Kuhn, R., Kinney, A.Y., Donaldson, G.W., Nakamura, Y., 2013. Reduction in salivary α-amylase levels following a mind–body intervention in cancer survivors—an exploratory study. Psychoneuroendocrinology 38, 1521–1531. https://doi.org/10.1016/J.PSYNEUEN.2012.12.021.
Liu, P.Z., Nusslock, R., 2018. Exercise-mediated neurogenesis in the hippocampus via BDNF. Front. Neurosci. 12, 332010. https://doi.org/10.3389/FNINS.2018.00052/BIBTEX.
Liu, K.K.L., Bartsch, R.P., Lin, A., Mantegna, R.N., Ivanov, P.C., 2015. Plasticity of brain wave network interactions and evolution across physiologic states. Front. Neural Circ. 9, 1–15. https://doi.org/10.3389/FNCIR.2015.00062/BIBTEX.
Lorenzetti, V., Allen, N.B., Fornito, A., Yücel, M., 2009. Structural brain abnormalities in major depressive disorder: a selective review of recent MRI studies. J. Affect. Disord. 117, 1–17. https://doi.org/10.1016/J.JAD.2008.11.021.
Love, M.F., Sharrief, A., Chaoul, A., Savitz, S., Beauchamp, J.E.S., 2019. Mind-body interventions, psychological stressors, and quality of life in stroke survivors: a systematic review. Stroke 50, 434–440. https://doi.org/10.1161/STROKEAHA.118.021150.
Maddock, C., Pariante, C.M., 2001. How does stress affect you? An overview of stress, immunity, depression and disease. Epidemiol. Psichiatr. Soc. 10 (3), 153–162. https://doi.org/10.1017/s1121189x00005285.
Malekpour, M., Shekouh, D., Safavinia, M.E., Shiralipour, S., Jalouli, M., Mortezanejad, S., Azarpira, N., Ebrahimi, N.D., 2023. Role of FKBP5 and its genetic mutations in stress-induced psychiatric disorders: an opportunity for drug discovery. Front. Psychiatr. 14, 1182345. https://doi.org/10.3389/fpsyt.2023.1182345.
Maruyama, Y., Kawano, A., Okamoto, S., Ando, T., Ishitobi, Y., Tanaka, Y., Inoue, A., Imanaga, J., Kanehisa, M., Higuma, H., Ninomiya, T., Tsuru, J., Hanada, H., Akiyoshi, J., 2012. Differences in salivary alpha-amylase and cortisol responsiveness following exposure to electrical stimulation versus the trier social stress tests. PLoS One 7, e39375. https://doi.org/10.1371/JOURNAL.PONE.0039375.
Mas-Bargues, C., Román-Domínguez, A., Borrás, C., Viña, J., 2023. Geroscience: a unifying view on aging as a risk factor. Aging: From Fundam. Biolo. Soc. Impact 587–600. https://doi.org/10.1016/B978-0-12-823761-8.00028-8.
Matousek, R.H., Pruessner, J.C., Dobkin, P.L., 2011. Changes in the cortisol awakening response (CAR) following participation in Mindfulness-Based Stress Reduction in women who completed treatment for breast cancer. Compl. Ther. Clin. Pract. 17, 65–70. https://doi.org/10.1016/J.CTCP.2010.10.005.
McEwen, B.S., 2000. Allostasis and allostatic load: implications for neuropsychopharmacology. Neuropsychopharmacology 22 (2 22), 108–124. https://doi.org/10.1016/s0893-133x(99)00129-3, 2000.
McEwen, B.S., 2005. Stressed or stressed out: what is the difference? J. Psychiatr. Neurosci. 30, 315.
Meier, M., Wirz, L., Dickinson, P., Pruessner, J.C., 2021. Laughter yoga reduces the cortisol response to acute stress in healthy individuals. Stress 24, 44–52. https://doi.org/10.1080/10253890.2020.1766018.
Miao, C., Gao, Y., Li, X., Zhou, Y., Chung, J.W. yee, Smith, G.D., 2023. The effectiveness of mindfulness yoga on patients with major depressive disorder: a systematic review and meta-analysis of randomized controlled trials. BMC Comple. Med. Ther. 23, 1–13. https://doi.org/10.1186/S12906-023-04141-2/FIGURES/6.
Miller, A.H., Pariante, C.M., 2020. Trial failures of anti-inflammatory drugs in depression. Lancet Psychiatr. 7, 837. https://doi.org/10.1016/S2215-0366(20)30357-6.
Miller, A.H., Raison, C.L., 2022. Burning down the house: reinventing drug discovery in psychiatry for the development of targeted therapies. Molecular Psych. Nature 28, 68–75. https://doi.org/10.1038/s41380-022-01887-y.
Moncrieff, J., Cooper, R.E., Stockmann, T., Amendola, S., Hengartner, M.P., Horowitz, M. A., 2022. SYSTEMATIC REVIEW the serotonin theory of depression: a systematic umbrella review of the evidence. https://doi.org/10.1038/s41380-022-01661-0.
Muehsam, D., Lutgendorf, S., Mills, P.J., Rickhi, B., Chevalier, G., Bat, N., Chopra, D., Gurfein, B., 2017. The embodied mind: a review on functional genomic and neurological correlates of mind-body therapies. Neurosci. Biobehav. Rev. 73, 165–181. https://doi.org/10.1016/J.NEUBIOREV.2016.12.027.
Muzik, M., Hamilton, S.E., Lisa Rosenblum, K., Waxler, E., Hadi, Z., 2012. Mindfulness yoga during pregnancy for psychiatrically at-risk women: preliminary results from a pilot feasibility study. Compl. Ther. Clin. Pract. 18, 235–240. https://doi.org/10.1016/J.CTCP.2012.06.006.
Naderi, M., Kordestani, H., Sahebi, Z., Khedmati Zare, V., Amani-Shalamzari, S., Kaviani, M., Wiskemann, J., Molanouri Shamsi, M., 2022. Serum and gene expression profile of cytokines following combination of yoga training and vitamin D supplementation in breast cancer survivors: a randomized controlled trial. BMC Wom. Health 22, 1–11. https://doi.org/10.1186/s12905-022-01671-8.
Naveen, G.H., Varambally, S., Thirthalli, J., Rao, M., Christopher, R., Gangadhar, B.N., 2016. Serum cortisol and BDNF in patients with major depression—effect of yoga. Int. Rev. Psychiatr. 28, 273–278. https://doi.org/10.1080/09540261.2016.1175419.
Nettis, M.A., Lombardo, G., Hastings, C., Zajkowska, Z., Mariani, N., Nikkheslat, N., Worrell, C., Enache, D., McLaughlin, A., Kose, M., Sforzini, L., Bogdanova, A., Cleare, A., Young, A.H., Pariante, C.M., Mondelli, V., 2021. Augmentation therapy with minocycline in treatment-resistant depression patients with low-grade peripheral inflammation: results from a double-blind randomised clinical trial. Neuropsychopharmacology 46 (5 46), 939–948. https://doi.org/10.1038/s41386-020-00948-6, 2021.
Nieuwenhuizen, A.G., Rutters, F., 2008. The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. Physiol. Behav. 94, 169–177. https://doi.org/10.1016/J.PHYSBEH.2007.12.011.
Niles, B.L., Mori, D.L., Polizzi, C.P., Pless Kaiser, A., Ledoux, A.M., Wang, C., 2016. Feasibility, qualitative findings and satisfaction of a brief Tai Chi mind-body programme for veterans with post-traumatic stress symptoms. https://doi.org/10.1136/bmjopen-2016.
Nugent, N.R., Brick, L., Armey, M.F., Tyrka, A.R., Ridout, K.K., Uebelacker, L.A., 2021. Benefits of yoga on IL-6: findings from a randomized controlled trial of yoga for depression. Behav. Med. 47, 21–30. https://doi.org/10.1080/08964289.2019.1604489.
Osimo, E.F., Baxter, L.J., Lewis, G., Jones, P.B., Khandaker, G.M., 2019. Prevalence of low-grade inflammation in depression: a systematic review and meta-analysis of CRP levels. Psychol. Med. 49, 1958–1970. https://doi.org/10.1017/S0033291719001454.
Öztürk, F.Ö., Bayraktar, E.P., Tezel, A., 2023. The effect of laughter yoga on loneliness, psychological resilience, and quality of life in older adults: a pilot randomized

controlled trial. Geriatr. Nurs. 50, 208–214. https://doi.org/10.1016/J.GERINURSE.2023.01.009.
O'Shea, M., Capon, H., Evans, S., Agrawal, J., Melvin, G., O'Brien, J., McIver, S., 2022a. Integration of hatha yoga and evidence-based psychological treatments for common mental disorders: an evidence map. J. Clin. Psychol. 78, 1671–1711. https://doi.org/10.1002/JCLP.23338.
O'Shea, M., Capon, H., Skvarc, D., Evans, S., McIver, S., Harris, J., Houston, E., Berk, M., 2022b. A pragmatic preference trial of therapeutic yoga as an adjunct to group cognitive behaviour therapy versus group CBT alone for depression and anxiety. J. Affect. Disord. 307, 1–10. https://doi.org/10.1016/J.JAD.2022.03.028.
Pal, R., Singh, S.N., Chatterjee, A., Saha, M., 2014. Age-related changes in cardiovascular system, autonomic functions, and levels of BDNF of healthy active males: role of yogic practice. Age 36, 1–17. https://doi.org/10.1007/S11357-014-9683-7/FIGURES/6.
Pariante, C.M., Lightman, S.L., 2008. The HPA axis in major depression: classical theories and new developments. Trends Neurosci. 31, 464–468. https://doi.org/10.1016/j.tins.2008.06.006.
Paulus, M.P., Stein, M.B., 2010. Interoception in anxiety and depression. Brain Struct. Funct. 214 (5 214), 451–463. https://doi.org/10.1007/S00429-010-0258-9, 2010.
Pizzagalli, D.A., Roberts, A.C., 2021. Prefrontal cortex and depression. Neuropsychopharmacology 47 (1 47), 225–246. https://doi.org/10.1038/s41386-021-01101-7, 2021.
Polyakova, M., Stuke, K., Schuemberg, K., Mueller, K., Schoenknecht, P., Schroeter, M.L., 2015. BDNF as a biomarker for successful treatment of mood disorders: a systematic & quantitative meta-analysis. J. Affect. Disord. 174, 432–440. https://doi.org/10.1016/J.JAD.2014.11.044.
Qu, S., Olafsrud, S.M., Meza-Zepeda, L.A., Saatcioglu, F., 2013. Rapid gene expression changes in peripheral blood lymphocytes upon practice of a comprehensive yoga program. PLoS One 8. https://doi.org/10.1371/journal.pone.0061910.
Quigley, K.S., Kanoski, S., Grill, W.M., Barrett, L.F., Tsakiris, M., 2021. Functions of interoception: from energy regulation to experience of the self. Trends Neurosci. 44, 29–38. https://doi.org/10.1016/J.TINS.2020.09.008.
Raison, C.L., Miller, A.H., 2003. When not enough is too much: the role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. Am. J. Psychiatr. 160 (9), 1554–1565. https://doi.org/10.1176/appi.ajp.160.9.1554.
Raison, C.L., Miller, A.H., 2013. Malaise, melancholia and madness: the evolutionary legacy of an inflammatory bias. Brain Behav. Immun. 31, 1–8. https://doi.org/10.1016/J.BBI.2013.04.009.
Raison, C.L., Knight, J.M., Pariante, C., 2018. Interleukin (IL)-6: a good kid hanging out with bad friends (and why sauna is good for health). Brain Behav. Immun. 73, 1–2. https://doi.org/10.1016/J.BBI.2018.06.008.
Rex, C.S., Lin, C.Y., Kramár, E.A., Chen, L.Y., Gall, C.M., Lynch, G., 2007. Brain-derived neurotrophic factor promotes long-term potentiation-related cytoskeletal changes in adult Hippocampus. J. Neurosci. 27, 3017–3029. https://doi.org/10.1523/JNEUROSCI.4037-06.2007.
Robinson, D.N., Hopke, T., Massey-Abernathy, A., 2023. Learning to relax: the impact of brief biofeedback training and gentle yoga on salivary cortisol reduction. Curr. Psychol. 42, 6980–6989. https://doi.org/10.1007/S12144-021-02036-4/TABLES/3.
Russo, M.A., Santarelli, D.M., O'Rourke, D., 2017. The physiological effects of slow breathing in the healthy human. Breathe 13, 298–309. https://doi.org/10.1183/20734735.009817.
Sandberg, E., Duberg, A., Lorenzon Fagerberg, U., Mörelius, E., Särnblad, S., 2022. Saliva cortisol in girls with functional abdominal pain disorders: a randomized controlled dance and yoga intervention. Front. Pediatr. 10, 836406. https://doi.org/10.3389/FPED.2022.836406/BIBTEX.
Sangeethalaxmi, M.J., Hankey, A., 2023. Impact of yoga breathing and relaxation as an add-on therapy on quality of life, anxiety, depression and pulmonary function in young adults with bronchial asthma: a randomized controlled trial. J. Ayurveda Integr. Med. 14, 100546. https://doi.org/10.1016/J.JAIM.2022.100546.
Santaella, D.F., Balardin, J.B., Afonso, R.F., Giorjiani, G.M., Sato, J.R., Lacerda, S.S., Amaro, E., Lazar, S., Kozasa, E.H., 2019. Greater anteroposterior default mode network functional connectivity in long-term elderly yoga practitioners. Front. Aging Neurosci. 10, 456503. https://doi.org/10.3389/FNAGI.2019.00158/BIBTEX.
Scangos, K.W., State, M.W., Miller, A.H., Baker, J.T., Williams, L.M., 2023. New and emerging approaches to treat psychiatric disorders. Nat. Med. 29, 317–333. https://doi.org/10.1038/s41591-022-02197-0.
Sevinc, G., Hölzel, B.K., Hashmi, J., Greenberg, J., McCallister, A., Treadway, M., Schneider, M.L., Dusek, J.A., Carmody, J., Lazar, S.W., 2018. Common and dissociable neural activity after mindfulness-based stress reduction and relaxation response programs. Psychosom. Med. 80, 439–451. https://doi.org/10.1097/PSY.0000000000000590.
Shaffer, F., Ginsberg, J.P., 2017. An overview of heart rate variability metrics and norms. Front. Public Health 5, 258. https://doi.org/10.3389/fpubh.2017.00258.
Shaffer, C., Westlin, C., Quigley, K.S., Whitfield-Gabrieli, S., Barrett, L.F., 2022. Allostasis, action, and affect in depression: insights from the theory of constructed emotion, 18, 553–580. https://doi.org/10.1146/ANNUREV-CLINPSY-081219-115627.
Shinba, T., Inoue, T., Matsui, T., Kimura, K.K., Itokawa, M., Arai, M., 2020. Changes in heart rate variability after yoga are dependent on heart rate variability at baseline and during yoga: a study showing autonomic normalization effect in yoga-naïve and experienced subjects. Int. J. Yoga 13, 160. https://doi.org/10.4103/IJOY.IJOY_39_19.
Siesser, W.B., Sachs, B.D., Ramsey, A.J., Sotnikova, T.D., Beaulieu, J.-M., Zhang, X., Caron, M.G., Gainetdinov, R.R., 2012. Chronic SSRI treatment exacerbates serotonin deficiency in humanized Tph2 mutant mice. https://doi.org/10.1021/cn300127h.
Sieverdes, J.C., Mueller, M., Gregoski, M.J., Brunner-Jackson, B., McQuade, L., Matthews, C., Treiber, F.A., 2014. Effects of hatha yoga on blood pressure, salivary α-Amylase, and cortisol function among normotensive and prehypertensive youth. J. Alternative Compl. Med. 20, 241–250. https://doi.org/10.1089/ACM.2013.0139/FORMAT/EPUB.
Silverman, M.N., Sternberg, E.M., 2012. Glucocorticoid regulation of inflammation and its functional correlates: from HPA axis to glucocorticoid receptor dysfunction. Ann. N. Y. Acad. Sci. 1261, 55–63. https://doi.org/10.1111/J.1749-6632.2012.06633.X.
Singleton, M., 2010. Yoga Body: the Origins of Modern Posture Practice. Oxford University Press.
Sloan, E.K., Capitanio, J.P., Tarara, R.P., Mendoza, S.P., Mason, W.A., Cole, S.W., 2007. Social stress enhances sympathetic innervation of primate lymph nodes: mechanisms and implications for viral pathogenesis. J. Neurosci. 27, 8857–8865. https://doi.org/10.1523/JNEUROSCI.1247-07.2007.
Sockol, L.E., Neill Epperson, C., Barber, J.P., 2011. A meta-analysis of treatments for perinatal depression. https://doi.org/10.1016/j.cpr.2011.03.009.
Streeter, C.C., Gerbarg, P.L., Saper, R.B., Ciraulo, D.A., Brown, R.P., 2012. Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. Med. Hypotheses 78, 571–579. https://doi.org/10.1016/J.MEHY.2012.01.021.
Tafet, G.E., Nemeroff, C.B., 2016. The links between stress and depression: psychoneuroendocrinological, genetic, and environmental interactions. J. Neuropsychiatry Clin. Neurosci. 28, 77–88. https://doi.org/10.1176/APPI.NEUROPSYCH.15030053/ASSET/IMAGES/LARGE/APPI.NEUROPSYCH.15030053F3.JPEG.
Taren, A.A., Gianaros, P.J., Greco, C.M., Lindsay, E.K., Fairgrieve, A., Brown, K.W., Rosen, R.K., Ferris, J.L., Julson, E., Marsland, A.L., Bursley, J.K., Ramsburg, J., Creswell, J.D., 2015. Mindfulness meditation training alters stress-related amygdala resting state functional connectivity: a randomized controlled trial. Soc. Cognit. Affect Neurosci. 10, 1758–1768. https://doi.org/10.1093/SCAN/NSV066.
Taylor, A.G., Goehler, L.E., Galper, D.I., Innes, K.E., Bourguignon, C., 2010. Top-down and bottom-up mechanisms in mind-body medicine: development of an integrative framework for psychophysiological research. Explore 6, 29–41. https://doi.org/10.1016/J.EXPLORE.2009.10.004.
Terhaar, J., Viola, F.C., Bär, K.J., Debener, S., 2012. Heartbeat evoked potentials mirror altered body perception in depressed patients. Clin. Neurophysiol. 123, 1950–1957. https://doi.org/10.1016/J.CLINPH.2012.02.086.
Thirthalli, J., Naveen, G.H., Rao, M.G., Varambally, S., Christopher, R., Gangadhar, B.N., 2013. Cortisol and antidepressant effects of yoga. Indian J. Psychiatr. 55. https://doi.org/10.4103/0019-5545.116315.
Tolahunase, M., Sagar, R., Dada, R., 2017. Impact of yoga and meditation on cellular aging in apparently healthy individuals: a prospective, open-label single-arm exploratory study. Oxid. Med. Cell. Longev. https://doi.org/10.1155/2017/7928981, 2017.
Turkheimer, F.E., Veronese, M., Mondelli, V., Cash, D., Pariante, C.M., 2023. Sickness behaviour and depression: an updated model of peripheral-central immunity interactions. Brain Behav. Immun. 111, 202–210. https://doi.org/10.1016/J.BBI.2023.03.031.
Tyagi, A., Cohen, M., 2016. Yoga and heart rate variability: a comprehensive review of the literature. Int. J. Yoga 9, 97. https://doi.org/10.4103/0973-6131.183712.
Uddin, L.Q., 2014. Salience processing and insular cortical function and dysfunction. Nat. Rev. Neurosci. 16 (1 16), 55–61. https://doi.org/10.1038/nrn3857, 2014.
Uebelacker, L.A., Battle, C.L., Sutton, K.A., Magee, S.R., Miller, I.W., 2016. A pilot randomized controlled trial comparing prenatal yoga to perinatal health education for antenatal depression. Arch. Womens Ment. Health 19, 543–547. https://doi.org/10.1007/S00737-015-0571-7/TABLES/2.
van Aalst, J., Ceccarini, J., Demyttenaere, K., Sunaert, S., Van Laere, K., 2020. What has neuroimaging taught us on the neurobiology of yoga? A review. Front. Integr. Neurosci. 14, 536683. https://doi.org/10.3389/FNINT.2020.00034/BIBTEX.
Videbech, P., 2000. PET measurements of brain glucose metabolism and blood flow in major depressive disorder: a critical review. Acta Psychiatr. Scand. 101, 11–20. https://doi.org/10.1034/J.1600-0447.2000.101001011.X.
Videbech, P., Ravnkilde, B., 2004. Hippocampal volume and depression: a meta-analysis of MRI studies. Am. J. Psychiatr. 161, 1957–1966. https://doi.org/10.1176/APPI.AJP.161.11.1957/ASSET/IMAGES/LARGE/N43F3.JPEG.
Villemure, C., Čeko, M., Cotton, V.A., Bushnell, M.C., 2014. Insular cortex mediates increased pain tolerance in yoga practitioners. Cerebr. Cortex 24, 2732–2740. https://doi.org/10.1093/CERCOR/BHT124.
Vollbehr, N.K., Hoenders, H.J.R., Bartels-Velthuis, A.A., Nauta, M.H., Castelein, S., Schroevers, M.J., Stant, A.D., Albers, C.J., de Jong, P.J., Ostafin, B.D., 2022. Mindful yoga intervention as add-on to treatment as usual for young women with major depressive disorder: results from a randomized controlled trial. J. Consult. Clin. Psychol. 90, 925–941. https://doi.org/10.1037/CCP0000777.
Vreeburg, S.A., Hoogendijk, W.J.G., Van Pelt, J., DeRijk, R.H., Verhagen, J.C.M., Van Dyck, R., Smit, J.H., Zitman, F.G., Penninx, B.W.J.H., 2009. Major depressive disorder and hypothalamic-pituitary-adrenal Axis activity: results from a large cohort study. Arch. Gen. Psychiatr. 66, 617–626. https://doi.org/10.1001/ARCHGENPSYCHIATRY.2009.50.
Wadden, K.P., Snow, N.J., Sande, P., Slawson, S., Waller, T., Boyd, L.A., 2018. Yoga practitioners uniquely activate the superior parietal lobule and supramarginal gyrus during emotion regulation. Front. Integr. Neurosci. 12, 328363. https://doi.org/10.3389/FNINT.2018.00060/BIBTEX.
Wahyuni, N., Adiputra, N., Putu, I., Adiatmika, G., Putu, L., Sundari, R., Indrayani, A.W., 2023. Effectiveness of Yoga in reducing IL-6 serum level in elderly with knee osteoarthritis. Bali Med. J. 12, 2463–2468. https://doi.org/10.15562/BMJ.V12I3.3386.

Wielgosz, J., Schuyler, B.S., Lutz, A., Davidson, R.J., 2016. Long-term mindfulness training is associated with reliable differences in resting respiration rate. Sci. Rep. 6 (1 6), 1–6. https://doi.org/10.1038/srep27533, 2016.

Witek-Janusek, L., Albuquerque, K., Chroniak, K.R., Chroniak, C., Durazo-Arvizu, R., Mathews, H.L., 2008. Effect of mindfulness based stress reduction on immune function, quality of life and coping in women newly diagnosed with early stage breast cancer. Brain Behav. Immun. 22, 969–981. https://doi.org/10.1016/J.BBI.2008.01.012.

Won, E., Kim, Y.-K., 2016. Stress, the autonomic nervous system, and the immune-kynurenine pathway in the etiology of depression. Curr. Neuropharmacol. 14, 665–673. https://doi.org/10.2174/1570159X14666151208113.

Woodward, A., Bullard, K., Taylor, R., Chatters, L., Baser, R., Perron, B., Jackson, J., 2009. Use of complementary and alternative medicines for mental and substance use disorders: a comparison of African Americans, black Caribbeans, and non-Hispanic whites. Psychiatr. Serv. 60, 1342. https://doi.org/10.1176/APPI.PS.60.10.1342.

Ying, S.W., Futter, M., Rosenblum, K., Webber, M.J., Hunt, S.P., Bliss, T.V.P., Bramham, C.R., 2002. Brain-derived neurotrophic factor induces long-term potentiation in intact adult Hippocampus: requirement for ERK activation coupled to CREB and upregulation of arc synthesis. J. Neurosci. 22, 1532. https://doi.org/10.1523/JNEUROSCI.22-05-01532.2002.

Yuvarani, G., Manoranjitham, R., Tharani, G., Kamatchi, K., Vaishnavi, G., 2020. A study to compare the effects of aerobic exercises and yoga on depression and maternal anxiety orienting among primiparous women. Biomedicine 40, 395–398. https://doi.org/10.51248/.V40I3.38.

Zannas, A.S., Jia, M., Hafner, K., Baumert, J., Wiechmann, T., Pape, J.C., Arloth, J., Ködel, M., Martinelli, S., Roitman, M., Röh, S., Haehle, A., Emeny, R.T., Iurato, S., Carrillo-Roa, T., Lahti, J., Räikkönen, K., Eriksson, J.G., Drake, A.J., Waldenberger, M., Wahl, S., Kunze, S., Lucae, S., Bradley, B., Gieger, C., Hausch, F., Smith, A.K., Ressler, K.J., Müller-Myhsok, B., Ladwig, K.H., Rein, T., Gassen, N.C., Binder, E.B., 2019. Epigenetic upregulation of FKBP5 by aging and stress contributes to NF-κB-driven inflammation and cardiovascular risk. Proc. Natl. Acad. Sci. U. S. A. 166, 11370–11379. https://doi.org/10.1073/PNAS.1816847116/SUPPL_FILE/PNAS.1816847116.SD10.XLSX.

Žebeljan, I., Lučovnik, M., Dinevski, D., Lackner, H.K., Moertl, M.G., Vesenjak Dinevski, I., Mujezinović, F., 2022. Effect of prenatal yoga on heart rate variability and cardio-respiratory synchronization: a prospective cohort study. J. Clin. Med. 11, 5777. https://doi.org/10.3390/JCM11195777, 11, 5777 2022.

Zelano, C., Jiang, H., Zhou, G., Arora, N., Schuele, S., Rosenow, J., Gottfried, J.A., 2016. Nasal respiration entrains human limbic oscillations and modulates cognitive function. J. Neurosci. 36, 12448–12467. https://doi.org/10.1523/JNEUROSCI.2586-16.2016.

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