REVIEW

DOI: http://dx.doi.org/10.15403/jgld-4867

Yoga Therapy in Functional Dyspepsia. A Narrative Reviews

Garima Setia[1,2,3], Ananda Balayogi Bhavanani[1,2,3], Meena Ramanathan[1,2,3], Nilakantan Ananthakrishnan[2], Vinod Vinoth[4], B. Sajeeth Manikanda Prabu[2,5], Balanehru Subramanian[2,6]

1) Institute of Salutogenesis & Complementary Medicine, Pondicherry;
2) Sri Balaji Vidyapeeth Deemed-to-be University, Pondicherry;
3) School of Yoga Therapy, Pondicherry
4) Department of Gastroenterology, Aarupadai Veedu Medical College & Hospital, Pondicherry;
5) Medical Gastroenterology, Mahatma Gandhi Medical College & Research Institute, Pondicherry;
6) School of Biological Sciences, SBV Deemed-to-be University, Pondicherry, India

Address for correspondence:
Ananda Balayogi Bhavanani
Institute of Salutogenesis & Complementary Medicine, Sri Balaji Vidyapeeth Deemed-to-be University, Pondicherry, India
yognat@gmail.com

Received: 20.02.2023
Accepted: 14.06.2023

ABSTRACT

Functional dyspepsia (FD) is a common upper gastrointestinal disorder, characterized by bothersome epigastric pain or burning, fullness after meals or early satiety. The precise pathophysiology remains incompletely understood but may include the role of disordered gut-brain communication leading to disturbances in gastro-duodenal physiological functioning. Even if there are several pharmacological treatment options, it is a chronic and relapsing disorder with persistent symptoms that makes its management difficult. Yoga is a fast-spreading complementary and alternative medicine (CAM) specialty, that has gained attention in the medical field for its ability to address the physical, emotional, mental and social aspects of health and disease. Various other CAM therapies are being used for FD with varying efficacy. However, apart from one research study that used yoga therapy on abdominal pain related functional gastrointestinal disorders in children which included a few FD cases as well (11.6%), no other study using yoga therapy has been done in FD as per our best knowledge. Therefore, in the present review, we have summarized the current scientific understanding of the probable effects of yoga on the pathophysiological mechanisms involved in FD (gastric motility, fundic accommodation, hypersensitivity, duodenal inflammation, psychological distress and gut-brain dysfunction). The literature suggests yoga can have a beneficial role in the management of FD. However, rigorous research and clinical trials are required to confirm the same.

Key words: yoga – yoga therapy – functional dyspepsia – gut-brain axis – hypothalamus-pituitary axis – vagus nerve.

Abbreviations: AG: acylated ghrelin; CAM: complementary and alternative medicine; CNS: central nervous system; CRH: corticotropin releasing hormone; CRP: C-reactive protein; DAG: des-acylated ghrelin; DGBI: disorder of gut-brain interaction; ENS: enteric nervous system; EPS: epigastric pain syndrome; FD: functional dyspepsia; FGID: functional gastrointestinal disorder; GABA: gamma-aminobutyric acid; GBA: gut-brain axis; *H. pylori: Helicobacter pylori*; HPA: hypothalamus-pituitary axis; HRA: heart rate variability; IL: interleukin; INF-γ: interferon-gamma; NANC: non-adrenergic non-cholinergic; NF-κB: nuclear factor kappa B; NO: nitric oxide; PDS: postprandial distress syndrome; PPI: proton pump inhibitor; RCA: randomized controlled trial; RSA: respiratory sinus arrhythmia; TCA: tricyclic antidepressants; TM: transcendental meditation; TNF-α: tumor necrosis factor alpha; 5HIAA: 5-hydroxyindoleacetic acid; 5-HT: 5-hydroxytryptamine.

INTRODUCTION

Functional dyspepsia (FD) is one of the most common disorders of gut-brain interaction (DGBI), previously known as functional gastrointestinal disorders (FGIDs) affecting the gastroduodenal region of the upper gastrointestinal tract [1]. Characteristic symptoms include epigastric pain, epigastric burning, postprandial fullness, and early satiety [2]. Associated symptoms such as bloating, belching, nausea, or vomiting may also be present [3].

Functional dyspepsia is diagnosed when no organic or structural causes are found during upper digestive endoscopy and Rome IV criteria are fulfilled that includes bothersome clinical symptoms [4]. However, low-grade duodenal inflammation is now considered an etiological factor in a subset of FD patients [5]. Approximately 70- 80% of individuals with dyspepsia have no structural explanation for their symptoms and have FD [2].

Rome-IV categorizes FD into broadly two categories: (i) epigastric pain syndrome (EPS) which includes presence of

bothersome epigastric pain or/and burning, at least once a week for 3 months with symptom onset at least 6 months prior; (ii) postprandial distress syndrome (PDS) which includes bothersome fullness after meals or/and early satiety present at least 2-3 days a week for 3 months with symptom onset at least 6 months prior [5, 6].

Epidemiology

According to the Rome Foundation global survey study, the worldwide prevalence of FD is 7.2% in Internet surveys covering 24 countries and 4.8% in household surveys covering 7 countries, thereby making it the most prevalent gastroduodenal disorder [7]. Prevalence in Asian countries is estimated to be 8-23 % [8]. Prevalence in India is estimated from community studies reporting the prevalence of uninvestigated dyspepsia. While a study from Mumbai reported prevalence to be 30.4% [9], another study from Chandigarh reported it at 7.5% [10]. Another Indian multicentric study reported the frequency of dyspeptic symptoms to be as high as 49% in the community [11]. Differences in the reported prevalence of dyspepsia can be due to variations in criteria or definition used for diagnosis [12] as well as cultural, dietary and socio-economic factors in different parts of the country.

Risk Factors

Studies suggest that female gender, smoking, non-steroidal anti-inflammatory drugs [13], acute gastrointestinal infections [14, 15], childhood abuse [16], psychological distress (including perceived stress [17], anxiety and depression [18] are risk factors for developing FD. Helicobacter pylori (H. pylori) infection was considered one of the risk factors; however, the Kyoto Global Consensus Meeting held in 2014 [19] suggested considering H. pylori-associated dyspepsia as a separate clinical entity as *H. pylori* eradication therapy only works in a minority of patients [20]. In Asia, heavy chili intake is implicated too [21].

PATHOPHYSIOLOGY

The pathophysiology of FD is not completely understood, and research is being carried out to understand mechanisms better for targeted therapy.

Gut Sensory and Motor Dysfunction

Functional dyspepsia has been attributed to various functional disturbances. Slow gastric and duodenal motility [5] are implicated in postprandial fullness, nausea and vomiting while inability of fundus to completely relax (leading to impaired gastric accommodation) [1] is associated with early satiety and is found in 40% of patients [22]. Visceral hypersensitivity, i.e., hypersensitivity of the stomach or duodenum to distension [1] or acid exposure [23] is implicated in epigastric pain and occurs in about one-third of the cases.

All these physiological disturbances were considered to be idiopathic in nature; however, more recently it has been observed that these might be due to structural changes in the duodenum or secondary to duodenal inflammation.

Duodenal Inflammation

Low-grade duodenal inflammation is now considered as one of the reasons behind FD symptoms in at least a subset of patients. An infection, microbiome alteration or a food allergen may present itself as an antigen causing epithelial and mucosal barrier disruption, immune reaction and inflammation [5]. A type-2 helper cell response is activated in which eosinophils are recruited that may degranulate in some patients [1]. While eosinophil degranulation may impinge on nerve fibre causing pain sensation, circulating cytokines release into blood may invoke an anxiety or stress response leading to reduced gastric motility and visceral hypersensitivity. Duodenal inflammation and increased epithelial permeability may cause sensitivity to acid and induce reflex responses such as delayed gastric emptying and impaired fundic accommodation [24-26].

Psychological Distress

Psychological distress plays an important role in developing FD but ambiguity exists as to whether psychological distress precedes gut symptoms or is a result of already manifested gut symptoms. Many studies have found a causal role of anxiety and/or depression in the etiology [27, 28]; however other studies have now confirmed the existence of a bi-directional pathway in FD [29, 30]. A review suggested that 50% of cases of DGBI started with mood disorders such as stress, anxiety and depression; in the other 50% cases gut disorder preceded mood disorder [31]. Another review [5] suggested that in one-third of individuals, a mood disorder preceded DGBI, and in two-thirds gastrointestinal disorder preceded mood disorder.

Disorder of Gut-Brain Axis

Rome-IV in 2016 changed the definition of FGIDs and renamed them as DGBI [32]. The connection between the central nervous system (CNS) and the enteric nervous system (ENS), is referred to as the gut-brain axis (GBA). It enables the bidirectional connection between the brain and the gastrointestinal tract via neural (sympathetic and parasympathetic branches of autonomic nervous system), neuroendocrine (hypothalamus-pituitary axis), immune (cytokines) and humoral pathways to communicate between the CNS and the ENS [33].

Any psychological or physiological stressor can disrupt the GBA which then alters normal gastric functioning and may lead to mood disorders, often seen in FD. The alteration in GBA can happen in both ways, i.e., (i) from gut to brain, and (ii) from brain to gut.

The hypothalamus is affected by the limbic system (whose main function is to regulate emotions) thus altering the hypothalamus-pituitary axis (HPA) and thereby BGA when faced with psychological stressors. Similarly, gut when faced with physiological stressors of any kind such as infection or an allergen, triggers immune responses thereby altering gut-brain axis. Gut microbiota too interacts with CNS via vagal pathways and any disturbance in it may lead to dysregulation in GBA also termed as microbiota-gut-brain axis [31].

TREATMENT

According to the American College of Gastroenterology (ACG) and Canadian Association of Gastroenterology (CAG)

joint guidelines released in 2017, *H. pylori* eradication therapy should be given if *H. pylori* is found positive in non-invasive testing or proton-pump inhibitors (PPIs) should be given in *H. pylori* negative cases or in those refractory to *H. pylori* treatment, as a first-line treatment [34]. In patients not responding to PPIs or *H. pylori* eradication therapy, tricyclic antidepressants (TCA) should be given, if required [34]. Interestingly ACG/CAG guidelines indicate the use of TCAs before using prokinetics in FD patients; however, in uninvestigated dyspepsia patients TCAs are given if prokinetics fail [4]. Functional dyspepsia patients not responding to PPIs, *H. pylori* eradication therapy or TCA therapy should be offered prokinetic therapy [34]. Functional dyspepsia patients not responding to drug therapy should be offered psychological therapies.

Though *H. pylori* test and treat approach versus empirical PPIs therapy showed no statistically significant difference in a meta-analysis of four randomized controlled trials (RCTs) [20], still it is recommended as a first-line approach because of cost efficacy and to prevent carcinomas in the long-term [35]. Proton pump inhibitors are superior to placebo in FD [36, 37]. As per a Cochrane review conducted by Pinto-Sanchez et al. [36] with sixteen eligible studies, PPIs therapy was slightly more effective than placebo, with 30% of the PPIs group reporting no or minimal symptoms compared with 25% of the placebo group (risk ratio of remaining dyspeptic 0.88, 95%CI: 0.82-0.94; p<0.001) with a number needed to treat of 13. This result was found to be independent of the doses or duration of treatment. There was also no difference when sub-grouped by *H. pylori* status, country of origin, or Rome III subtypes as opposed to a systematic review conducted by Wang in 2007 [37] that considered subgroups such as dysmotility type, ulcer-like dyspepsia, reflux like dyspepsia based on Rome II criteria for the inclusion of studies. In the same study PPIs (40.3%) were more effective compared with placebo (32.7%), yielding a relative risk reduction of 10.3% (95%CI, 2.7-17.3%, p<0.005). The estimated number needed to treat was 14.6 patients (95%CI: 8.7–57.1 patients).

Given evidence of impaired duodenal clearance of gastric acid and duodenal hypersensitivity to infused gastric acid in individuals with FD acid-suppression therapy is a logical treatment [23]. However, they have risks with long-term use [38] and are most useful only in a subset of patients, in those with epigastric pain [5, 39]. Nonetheless, recent studies have also pointed out to their beneficial role in PDS [36]. Sanaka et al. [40] in their review suggested that PPIs delayed the gastric emptying of solid meals as they impaired hydrolytic digestion by inhibiting acid-dependent peptic activity. Prokinetics help postprandial distress more than epigastric pain or burning. But they must be used with caution as few of these drugs prolong QT interval [2]. Cisapride has been shown to be effective in FD; however, has been withdrawn due to increased cardiac events [41]. Metoclopramide too has been associated with tardive dyskinesia [4]. Tricyclic antidepressants such as amitriptyline and imipramine were found to be effective but not selective serotonin reuptake inhibitors [42]. Trials for psychotherapy have provided dichotomous outcomes [4]. A meta-analysis of four trials [34] two of which used cognitive behavioral therapy suggested benefit in reducing persistent symptoms (RR=0.53; 95%CI: 0.44-0.65).

Given the limited efficacy of the aforementioned pharmacologic therapies, it is estimated that approximately 50% of patients with gastrointestinal symptoms try complementary and alternative medicine (CAM) therapies for symptom relief [43, 44]. These therapies that have been used in FD include herbal medicines [45-47], acupuncture [48-50], and hypnotherapy [51, 52] with varying degrees of efficacy. Also, these studies have been limited to certain ethnic population. For example, rikkunoshito, a Japanese herbal medicine, has been used in trials limited to the Japanese population. Acupuncture has been widely practiced in China and Japan [53] and though now is being accepted in western population as well, its trials in Chinese population have been beneficial while it has failed to do so in western population [54]. This limits the generalization of results. A review study on CAM therapies for FD suggested that though some RCTs have proven the efficacy of CAM therapies in DGBIs, additional RCTs are required to make any recommendations for CAM therapies in managing FD [55].

Yoga Therapy

Yoga is an ancient Indian practice of self-transformation and self-realization. It comprises a group of physical, mental, and spiritual practices that aims at purifying, strengthening, and integrating mind, body, and soul for achieving complete state of health and wellness. In yoga, it is said that "loss of the connection with self is the main cause that creates disease" [56], which one seeks to establish through yoga.

Doctor B. Ramamurthy, an eminent neurosurgeon suggested that yoga practices re-orient functional hierarchy of the entire nervous system. He further specified that it not only benefits the nervous system but also cardiovascular, respiratory, digestive, and endocrine systems [57].

Although yoga was traditionally used to achieve the highest state of consciousness, its components are now being used as a therapeutic modality. Yoga therapy uses specific techniques to restore health and overall wellness of individuals. It is a whole-person approach and targets the entire human being rather than a particular body system or organ.

According to the International Association of Yoga Therapists (IAYT), yoga therapy is "the professional application of the principles and practices of yoga to promote health and well-being within a therapeutic relationship that includes personalized assessment, goal setting, lifestyle management, and yoga practices for individuals or small groups" [58]. It further states the goals of Yoga therapy include eliminating, reducing, or managing symptoms that cause suffering; improving function; helping to prevent the occurrence or reoccurrence of underlying causes of illness; and moving toward improved health and well-being.

The beneficial role of yoga in mood disorders such as stress, anxiety and depression is well established [59-61]. Yoga has also been found to be beneficial in cardiovascular, respiratory, auto-immune, metabolic and musculoskeletal disorders [62, 63].

Possible Role of Yoga in FD

Though role of yoga therapy in FD is quite unexplored, we have broken down the research on yoga with regard to individual pathophysiological mechanisms involved in FD such as gastric motility, visceral hypersensitivity, psychological

distress/mood disorders, altered CNS processing, dysfunction in gut-brain axis and the possible role yoga can play in these underlying mechanisms. A summarized form is presented in Table I.

Possible Role of Yoga in Gastric Motility

One main reason recognized behind altered gastric motility is stress which results in the activation of brainstem corticotropin-releasing factor (CRF) receptors as part of stress

Table I. Role of yoga in various underlying mechanisms of FD

S.No.	Pathophysiology	Implications	Probable Causes/Mechanisms	How Yoga can help
1.	Impaired gastric & duodenal motility	Altered gastric emptying Altered Intestinal reflex activity Increased chemosensitivity and mechanosensitivity	Stress induced - SNS decreases gastric motility but increases colonic motility [65] Reduced vagal tone [66,67] Altered ghrelin levels [84] Duodenal inflammation (Discussed below in point 4)	Activation of PNS and decreasing SNS activity [71] Enhancing vagal tone [72,73] Increased UAG and decreased AG levels [89] Regulate immune mechanisms
2.	Impaired Gastric accomodation	Impaired fundus accommodation Increased antrum distension (degree of antral distension is related to severity of FD symptoms) Associated with early satiety	Fundic smooth muscles fail to relax [90] Duodeno-gastric reflex to increased exogenous acid in the duodenum [103] Role of anxiety [108,109]	Increased NO levels [99,100] may help in relaxing fundic smooth muscles Decreased acid levels [106] Reduced anxiety [148–150]
3.	Visceral Hypersensitivity	Increased sensation of pain and burning Altered intestinal reflexes	Reduced anti- nociceptive role of the vagus nerve [110] Altered CNS pain processing [113] Sensitization in the central and autonomic (vagal, spinal) or enteric nervous systems resulting in hyperexcitability [165] Decreased acid clearance from proximal duodenum due to decreased gastro-duodenal motility Local immune activation causing impaired epithelial barrier also responsible for hypersensitivity (further discussed in point 4)	Enhanced vagal nerve tone [72–74] Lessened pain perception has been found in meditators and Yoga practitioners owing to decreased activity in regions of pain perception [166] Autonomic response to pain are altered in Yoga practitioners [167]. Mind-body practices including Yoga, guided imagery, hypnosis have shown positive influence in pain states. [168] The major inhibitory neuron GABA may play a key role in central inhibition and is also implicated in pain control. Studies suggest increase in GABA levels with Yoga [70,123,124]. Yoga may help enhance gastro-duodenal motility by increasing vagal tone (Discussed in point 1)
4.	Duodenal inflammation	Eosinophilic granulation causing nerve firing and pain May also lead to delayed gastric emptying as a part of gastro-duodenal reflex and immune mechanism Weak mucosal barrier	Allergen or infection or psychological stress may trigger immune response causing systemic alterations such as increased levels of circulating cytokines & small intestinal T cells. Acute psychological stress that causes mast cell activation mediated by CRH results in duodenal mucosal permeability [139] Impaired serotonin induced ion secretion in response to duodenal acid infusion —> impaired bicarbonate flux —> impaired mucosal barrier	Reduction in pro-inflammatory cytokines (IL-6, IL-2, IL- 1β, CRP, TNF-α and IFN-g as well as pro-inflammatory transcription factor NF-κB) [128–130,135] Reduction in cortisol levels Changed mucosal pattern of stomach [140] Increased serotonin levels [143,144]
5.	Mood Disorders (Stress, Depression & Anxiety)	Activation of SNS (neural) - release of, HPA (neuroendocrine) - release of CRH>ACTH> Cortisol, immune pathways Weak mucosal barrier	Environmental factors, childhood abuse, genetic predisposition, Work or family related	Increased GABA levels in the thalamus correlated with improved mood [123,124] Reduction in cortisol levels [78–80,135] Reduction in stress, depression and anxiety symptoms [152,153,156,157,169,170]
6.	GBA axis dysfunction	Microbiota alteration (could precede also) All above pathophysiological changes (Discussed in point 1-5)	Microbiota alteration Psychological (Brain-Gut) or physiological stressors such as infection, inflammation (Gut-brain)	Meditation has shown positive results in enhancing beneficial bacteria [163,164] Bidirectional role in the regulation of GBA, i.e., from top-down as well as bottom-up pathway by enhancing psychological health [148,156–158,169] as well as addressing gut health [69,164,171–173] .

SNS: sympathetic nervous system; PNS: parasympathetic nervous system; UAG: unacylated ghrelin; AG: acylated ghrelin; NO: nitric oxide; CNS: central nervous system; GABA - γ-aminobutyric-acid; IL: interleukin; CRP: C-reactive protein; TNF-α: tumor necrosis factor-alpha; IFN-γ: Interferon-gamma; NF-κB - nuclear factor kappa B ; CRH: corticotropin releasing hormone; HPA: hypothalamus pituitary axis; ACTH: adrenocorticotropic hormone; GBA: gut-brain axis.

response, that decreases gastric motility and inhibits gastric emptying [64, 65]. Any acute stressor be it psychological, environmental or physiological would result in stress response as it is critical for survival. However, rapid counter-regulation happens via vagal nerve once the threat situation is terminated. In states of chronic stress, the body is unable to return to a state of homeostasis. It has been suggested in patients with FD that the stress-induced decrease in antral motility could be associated with a decreased vagal tone, rather than an increased sympathetic tone [66, 67].

Yoga is hypothesized to work by downregulating sympathetic tone, HPA axis and increasing vagal tone [68–70]. Innes et al. [71] in their systematic review reported from 42 studies that over 85% of them offer some evidence of yoga promoting a reduction in sympathetic activation, enhancement of cardiovagal function, and a shift in the autonomic nervous system balance from primarily sympathetic to parasympathetic.

Since there is no direct way to measure vagal tone, research employ tools such as heart rate variability (HRA), respiratory sinus arrhythmia (RSA) that represent its increase or decrease. Bhavanani et al. [72] in their study on four different *Pranayama* reported greater RSA in the traditional ratio, *Pranava* and *Savitri* pranayamas as compared to *Sukha* pranayama. Another study done on 11 healthy yoga practitioners reported increased high-frequency component of HRV associated with increased vagal tone [73]. Raghuraj et al. [74] found significant increase in low frequency (LF) power of HRV following *kapalabhati* suggesting increased sympathetic activity.

Also, increased hypothalamic corticotropin-releasing hormone (CRH) levels have been reported in FD [75] and is implicated in inhibiting vagal efferent activity [76, 77]. The role of yoga in the reduction of cortisol has been studied in several studies. In a study done on 7 yoga instructors, mean serum cortisol decreased after the intervention which included 15 minutes of asana, pranayama, and 20 mins of Soham Meditation [78]. In another study on 59 early-stage breast and 10 prostate cancer patients, eight-week of mindfulness-based stress reduction (MBSR) meditation program led to a decrease in afternoon cortisol levels along with significant improvement in the quality of life, symptoms of stress and sleep quality [79].

Practice of transcendental meditation (TM) for 4 months decreased basal and average cortisol levels and increased cortisol responsiveness to stressors [80]. In another study on TM, participants with 3–5 years of experience had significantly greater decreases in cortisol levels than novices with 3–4 months of TM experience [81]. Decreased cortisol levels reported after yoga interventions indicate attenuation of the HPA axis by yoga [80].

Another reason behind altered gastric motility could be because of altered ghrelin level in FD patients. Ghrelin has a well-established role in increasing appetite and food intake and stimulating gastric motility [82, 83]. Plasma ghrelin levels in patients with FD are controversial. A study reported abnormally low ghrelin levels pre-prandial in FD patients (Rome-II criteria) and the absence of significant postprandial decrease of ghrelin levels in a subset of dysmotility-like FD patients [84]. Another study on FD patients (Rome-III criteria) found acylated ghrelin (AG) levels in PDS subgroup significantly lower than in healthy volunteers and no significant difference in des-acylated ghrelin (DAG) levels among EPS, PDS and healthy volunteers [85]. Yet another study observed elevated levels of AG in FD patients (Rome-II criteria) than healthy controls whereas the DAG form showed the opposite tendency [86].

Though plasma ghrelin levels varied across research in FD patients, research with extraneous ghrelin administration has shown encouraging results. In the research done on five FD (Rome II criteria) patients [87], ghrelin administration increased daily food intake by approximately 30%. It is important because a subset of FD patients report decreased appetite and food intake. In another study [88] improvement in upper gastrointestinal symptoms was observed in FD patients after administration of the traditional Japanese medicine rikkunoshito, accompanied by an increase in the plasma ghrelin levels. In another multicenter, randomized, placebo-controlled trial [47], rikkunoshito was found to be effective in decreasing dyspepsia symptoms in FD patients (Rome III criteria) with increased plasma ghrelin levels.

As per the author's best knowledge, only one study has been done on plasma ghrelin levels with yoga. In that particular follow-up study [89] done on metabolic syndrome patients, yoga practice significantly increased levels of total circulating ghrelin and unacylated ghrelin and decreased AG levels after 1 year of yoga training.

Possible Role of Yoga in Gastric Accommodation

Research suggests that reflex gastric accommodation to a meal is achieved via relaxation of the proximal stomach, mediated by vagus nerve [90, 91]. Stimulation of esophageal vagal afferents results in proximal gastric relaxation via either inhibition/withdrawal of tonic cholinergic vagal efferent pathways or activation of inhibitory non-adrenergic non-cholinergic (NANC) pathways [90,92].

Inhibitory NANC pathways responsible for relaxation of stomach involves neurotransmitters, vasoactive intestinal peptide and nitric oxide (NO). The gastric fundus tone is regulated by a balance between a stimulatory cholinergic input and an inhibitory influence from NANC transmitters including NO [93, 94]. In studies done to see the effect of NO synthase inhibition by l-NMMA on proximal gastric volume, it was found that l-NMMA decreased basal fundic volume and reduced fundic relaxation [95,96].

However, the use of NO donors for fundic accommodation dysfunction has shown mixed results [97,98]. While anticholinergic drugs improved the threshold for discomfort as well as maximum distension volume, NO donor nitroglycerin failed to modify thresholds though it improved tolerance in 2 out of 13 patients [97]. In another study sublingual administration of glyceryl trinitrate immediately before a meal improved the overall symptom score [98]. Owing to the significant side effects such as headaches associated with the use of nitrates, Kuiken et al. [95] suggested development of fundus relaxing drugs aimed at selectively activating NO producing neurons at the level of the myenteric plexus.

Studies with yoga as intervention have evaluated the nitric oxide levels in serum and have found significant results. In RCT study on 234 pregnant women, yoga training for twenty weeks significantly increased NO levels along with increase

in total power of HRV, baroreflex sensitivity, and decrease in interleukin-6 [99]. Another study on 200 healthy individuals found significantly elevated levels of plasma nitric oxide and reduction in heart rate, systolic blood pressure and diastolic blood pressure with 6 months of yoga training [100]. Yet another study on 40 volunteer subjects concluded that long-term Yoga practice promotes higher NO concentration in blood [101].

Another factor that can impair gastric accommodation is increased duodenal acid exposure, probably through triggering duodeno-gastric reflexes [102, 103]. Though studies suggest normal acid production in FD patients [104] and only an increase in the duodenal acid exposure due to slow motility, or impaired mucosal barrier, there are other studies which suggest increased acid production as well in a subset of patients [105].

In a pilot study done by Gharote [106], yoga cleansing technique *Vatasara* (air swallowing) resulted in marked decrease in total acidity. This particular has also been hypothesized for eradication of *H. pylori* infection [107]. However, no other study has been conducted with yoga on gastric acid levels. There are *Pranayama* (breathing) techniques such as *Shitali* and *Shitkari* in yoga, that are suggested traditionally for cooling down the body and removing excessive *Pitta* that is correlated to acid and bile levels in the body. However, no study has been conducted to elaborate on the mechanism which substantiates these claims and would require further investigation.

Further, there is evidence suggesting the role of anxiety in impaired gastric accommodation [108, 109]. Yoga has proven its efficacy in reducing anxiety and anxiety disorders which are detailed further below.

Possible Role of Yoga in Gastric Hypersensitivity

Reduced anti-nociceptive role of the vagus nerve [110], corticosterone-induced increased excitability of dorsal root ganglion neurons [66, 111], increased acid secretion [105] or increased acid exposure decreased due to slow gastroduodenal motility [112], as well as altered CNS pain processing [22, 113] are implicated in gastric hypersensitivity.

Impaired vagal function is associated with lower visceral sensory thresholds similar to those observed in vagotomy [110]. It has been found that vagal nerve stimulation (electric stimulation of the vagus nerve) has an anti-nociceptive effect [114, 115]. Therefore, enhancing vagal tone through yoga (research already discussed above) might have a positive effect. In an RCT, done on 40 FD patients, breathing exercises with vagal biofeedback (at 6 breaths/min, 5 min each day for 4 weeks) resulted in the improvement of drinking capacity and quality of life, but did not improve baseline vagal tone or intragastric volume [116].

Also, the anti-nociceptive effect of vagal nerve stimulation may rely on central inhibition [70, 114]. Gamma-aminobutyric acid (GABA) receptors in the thalamus are implicated in pain control [117, 118]. Though the levels of GABA are unaltered in FD patients [119], studies have shown improved FD symptoms with GABA receptor agonist in rat model [120] or GABA analog medicines [121]. Gamma-aminobutyric acid also has a role in inhibition of cortisol/CRH activity [122]. Some papers have suggested that yoga may lead to 27% increase in GABA levels immediately after a 60 min yoga session [123] or a 34% increase in thalamic GABA levels in experienced yoga practitioners and a 15% increase in novices with 12 weeks of yoga asana training [124]. At least once a week Yoga intervention may be necessary to maintain the elevated GABA levels [125].

Another mechanism that could be responsible for increased visceral hypersensitivity is local immune activation causing impaired epithelial and mucosal barrier also duodenal inflammation which may then become hypersensitive to acid. Stress also causes weak mucosal barrier. These are discussed below.

Possible Role of Yoga in Duodenal Inflammation and Weak Mucosal Barrier

The levels of circulating pro-inflammatory and anti-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin (IL)- 1β, IL-4, IL-5 and IL-13, IgE antibodies [66], as well as small-intestinal-homing T cells are increased in patients with FD and correlated with symptom intensity [126]. Growing evidence suggests that yoga therapy has immunomodulatory effects. Many studies, reviews, and meta-analyses have reiterated the beneficial effects of yoga in reducing inflammation and inflammatory markers. Morgan et al. [127] in their meta-analysis on mind-body therapies including tai chi, qui gong, or yoga found a small effect on decreasing inflammatory markers such as IL-6 and TNF–α. In a systematic review of 15 studies, 11 studies reported positive effects of yoga on inflammatory biomarkers. Analysis showed greater improvements in inflammation with increasing doses of yoga therapy [128]. Another review too recorded evidence for the benefits of yoga on levels of inflammatory markers, such as C-reactive protein (CRP), IL-1β, IL-6, TNF-α and interferon-gamma (INF-γ) as well as circulating cortisol and suggested use of Yoga as adjuvant therapy in conditions with an inflammatory component [129].

In a RCT on 200 breast cancer patients [130] lowered IL-6, TNF-α, IL-1β as well as higher vitality and lower fatigue were observed in the yoga group as compared to the control group. Another study on patients with chronic inflammatory diseases participants reported reduction in inflammatory markers including IL-6 and TNF-α with a short-term yoga-based lifestyle program for 10 days [131]. In a study on expert meditators, yoga was found to be beneficial in reducing pro-inflammatory cytokines including IL-6, IL-2, CRP, TNF-α and IFN-γ [132]. Yet another study [133] reported reduction in salivary concentrations of pro-inflammatory cytokines IL-1β, IL-8, and monocyte chemotactic protein -1 (MCP-1) after twenty minutes of yogic breathing.

Studies have also been done on genomic markers of inflammation. Bower and Irwin in their descriptive study [134] that included 26 RCTs of mind-body therapies including yoga, showed mixed effects on circulating inflammatory markers, including CRP and IL-6 but more consistent findings on genomic markers. Studies included in the above review showed decreased expression of inflammation-related genes and reduced signaling through the proinflammatory transcription factor, nuclear factor kappa B (NF-κB). In their review they observed that alterations in inflammatory gene expression were identified after relatively short 6-week interventions

while effects on non-specific markers, including circulating inflammatory markers took longer to emerge and required more intensive practice of the treatment. In a RCT on breast cancer patients [135], 12 weeks of Iyengar yoga program resulted in reduced activity of the pro-inflammatory transcription factor NF-κB. Though no significant changes in CRP or IL-6 were observed, plasma levels of soluble TNF receptor type II remained stable in the yoga group but increased in the control group. In another RCT [136] on 45 dementia caregivers, it was found that meditation reverses the pattern of increased NF-κB.

This is plausible as inflammatory responses are modulated via downregulating of HPA axis as well as moving the balance of autonomic nervous system towards parasympathetic tone. This leads to a greater sympatho-vagal balance which is thought to reduce inflammation via decreased adrenergic signaling [137] as well as a vagally mediated cholinergic anti-inflammatory pathway [138].

Stress can also lead to a weak mucosal barrier and an increase duodenal mucosal permeability via mast cell activation mediated by CRH [139]. Activation of SNS causes decreased mucosal secretion while PNS exerts both excitatory and inhibitory control over gastric and intestinal tone, motility and secretions [90]. Bhole [140] studied the changes in the mucosal pattern of stomach following anger and frustration in seven students undergoing physical training and reported that yoga and relaxation-cum-meditation could bring back the changed tone and changed mucosal pattern of stomach better than ordinary rest.

Also, in FD patients, serotonin-induced bicarbonate ion secretion, which plays a role in restoring ionic balance during acidification of duodenal lumen is reduced [141] that result in a compromised mucosal barrier. 5-hydroxytryptamine (5-HT) or serotonin content [measured as 5-hydroxyindoleacetic acid (5-HIAA) during a meal] studied immunohistochemically in duodenal mucosa of post-infectious FD patients with 6 months or more after the infection was found to be significantly reduced, but not in recovered controls [142]. Research suggests positive effects of yoga on serum 5-HT levels. Twelve weeks of yoga practice in premenopausal women maintained serum serotonin levels while the control group recorded a decrease [143]. In another study on university students, 12 weeks of yoga practice significantly increased plasma levels of serotonin compared with the control group [144]. In a study on mental depression cases, plasma serotonin levels increased after 3 and 6 months of Kundalini yoga practice [145]. In another study on polar sojourners, 10 months of daily yoga practice increased serotonin serum levels in the yoga group from 6.4±1.6 ng/mL to 6.6±0.4 ng/mL indicating a 3.1% increase, while no such increase was noticed in the control group [146].

Possible Role of Yoga in Psychological Distress/Mood Disorders

Considering the role of mood disorders such as stress, anxiety and depression in the etiology of at least 50% cases of DGBIs, it is important to look at the role, yoga can play in addressing them. Yoga has proven to be effective in controlling stress response, reducing anxiety and depression in numerous research worldwide. Studies suggest that stress-induced allostatic load is associated with increased sympathetic nervous system activity, increased HPA axis activity and decreased GABAergic activity [70]. Research also suggest that yoga practices reduce stress-induced allostatic load by increasing the parasympathetic nervous system activity, decreasing the HPA axis activity and increasing GABAergic activity in part through vagal stimulation [69, 70, 147].

Cramer et al. [148] in their systematic review and meta-analysis suggested that yoga might be an effective and safe intervention for individuals with elevated levels of anxiety. Another review concluded that although all studies reported positive findings for the use of yoga in anxiety but owing to methodological inadequacies more robust studies are required [149]. In a study observing the effects of mindfulness-based meditation on anxiety and depression in chronic pain patients, noticeable improvement in depression, anxiety and pain was found over a yearlong observation period [150]. In an RCT conducted on inflammatory bowel disorders (IBD) patients, to assess the effect of guided imagery with relaxation-training technique, yoga was found to decrease pain, stress as well as anxiety levels and improvement in mood and the quality of life, compared to wait-listing control group [151].

In another RCT conducted on patients with IBD, participation in the Breath-Body-Mind Workshop (BBMW) resulted in significant improvements in psychological (stress, anxiety & depression) and physical symptoms (inflammatory bowel disorders symptom score), quality of life, and CRP [152]. An RCT study involving 90 young healthcare students compared the effects of training in slow and fast *Pranayama* for 3 months. There was a reduction in perceived stress in both fast and slow *Pranayama* group [153].

Research papers have indicated increased breathing frequency and decreased depth of breathing in anxiety, vagal system deactivates while there is an activation of SNS [154]. Since the vagal tone can be influenced by breathing, hence it's plausible that increasing the depth of breathing and decreasing the breath frequency through *Pranayama* would help in the mitigation of stress and anxiety [155].

A systematic review of five RCTs reported yoga-based interventions to be effective in treating depression ranging from mild depressive symptoms to major depressive disorder [156]. In an RCT on 40 elderly women, yoga therapy for 60 mins twice a week reported decrease in levels of depression and anxiety after 3 months of intervention along with an increase in self-esteem [157]. In another study on young adults, with self-reported symptoms of depression and scores in the "mild mood disturbance" range on the BDI, five weekly sessions of Iyengar yoga resulted in reduction in scores of depression [158]. In another RCT involving 80 patients with a major depressive disorder, it was found that individuals receiving yoga therapy with standard medical therapy had significantly lower scores on depression, anxiety and the Clinical Global Impression (CGI) scale than those receiving only standard medical therapy after 30 days of intervention [159].

Possible Role of Yoga in Gut-Brain Axis

Yoga therapy can play a bidirectional role in the regulation of gut-brain axis, i.e., from top-down as well as bottom-up pathway (Fig. 1). The role of yoga therapy in psychological disorders such as stress, anxiety and depression is evident from

multiple high-quality research papers as already discussed above. Thus, it is likely to benefit symptoms of FD arising from brain-gut etiology. On the other hand, the beneficial role of yoga in decreasing inflammation and inflammatory markers is also coming to the forefront with recent research in various chronic inflammatory disorders. Hence, it might likely play a positive role in duodenal inflammation thus addressing the gut-brain pathway too. However, evidence-based research is required to see the effect of yoga in FD patients.

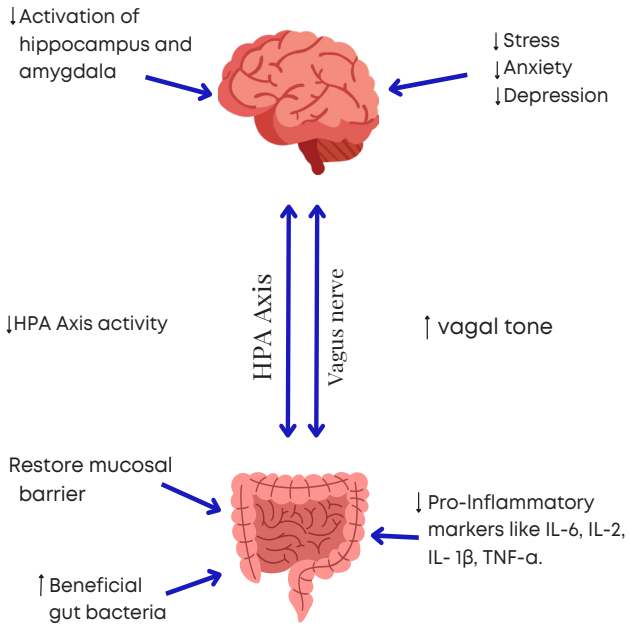

Fig. 1. Postulated effects of yoga at various levels of gut-brain interaction. HPA: hypothalamus-pituitary axis; IL: interleukin-2; TNF-α: tumor necrosis factor-alpha.

Additionally, the role of yoga in enhancing vagal tone and downregulating HPA axis has already been elaborated upon. Vagal nerve and HPA axis both are important link between CNS and ENS, and disturbance in them has been linked to altered gastro-duodenal sensory-motor function. However, research specific to yoga and FD is required to see the extent of benefit in FD population.

Yoga also has a direct effect on neural processes including modulating the activity of amygdala and hippocampus. Research indicate greater activation of the hippocampus, Para hippocampal gyrus, and amygdala, and lower activation of dorsal prefrontal cortex, insula, caudate, and cerebellum in FD patients with abuse history [160]. A decrease in volume and activity has been observed in the amygdala [161] and in the hippocampus [162] in practitioners of different styles of meditation.

Gut microbiota dysbiosis has also been implicated in FD patients. Meditation has been significantly correlated with the enrichment of three beneficial bacteria genera (*Bifidobacterium*, *Roseburia*, and *Subdoligranulum*) [163, 164].

CONCLUSIONS

Functional dyspepsia is a chronic and relapsing disorder that incurs significant healthcare costs and impairs quality of life significantly. Because of heterogeneity in etiology and symptoms and lack of patient-tailored therapy options, it is often difficult to treat especially with psychological associations. The definition, pathophysiology and treatment of FD has been constantly evolving and with the most recent Rome IV guidelines in 2016, the focus has been on evolving a biopsychosocial model for FD and other FGIDs. The need to integrate evidence-based brain-gut therapies within gastroenterology practice settings is now being recognized. Effective management requires a biopsychosocial approach that addresses the variability and complexity of patients who have these disorders. Complementary and alternative medicine therapies including yoga therapy use a more patient-centered approach. Yoga therapy is a holistic mind-body approach which can play a bidirectional role in modulating GBA. Though various CAM therapies have been used for managing FD, their usage is limited to certain ethnic population. Use of yoga therapy, however, would be novel in this direction. Also, in the present times when yoga is spreading fast worldwide and has recorded efficacy in various disorders irrespective of ethnicity or culture, it is pertinent to explore its role in the integrative management of FD. Yoga therapy is a non-drug, cost-effective adjuvant that can be easily integrated into daily life and practiced long-term thus preventing relapses.

Conflicts of interest: None to declare.

Author's contributions: G.S. and A.B.B. drafting the manuscript. All authors contributed to the design of the work, critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

Acknowledgements: This article was supported by the UGC-NET Junior Research Fellowship granted to the first author; hence we would like to extend our gratitude to the University Grants Commission. We would also like to thank Mr. G Dayanidy, Assistant Professor, ISCM for providing all the technical help and support.

REFERENCES

1 Talley NJ, Ford AC. Functional Dyspepsia. N Engl J Med 2015;373:1853–1863. doi:10.1056/NEJMra1501505
2 Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. The Lancet 2020;396:1689–1702. doi:10.1016/S0140-6736(20)30469-4
3 Tack J, Talley NJ. Functional dyspepsia--symptoms, definitions and validity of the Rome III criteria. Nat Rev Gastroenterol Hepatol 2013;10:134–141. doi:10.1038/nrgastro.2013.14
4 Black CJ, Houghton LA, Ford AC. Insights into the evaluation and management of dyspepsia: recent developments and new guidelines. Therap Adv Gastroenterol 2018;11:1756284818805597. doi:10.1177/1756284818805597
5 Talley NJ, Goodsall T, Potter M. Functional dyspepsia. Aust Prescr 2017;40:209–213. doi:10.18773/austprescr.2017.066
6 Stanghellini V, Chan FKL, Hasler WL, et al. Gastroduodenal Disorders. Gastroenterology 2016;150:1380–1392. doi:10.1053/j.gastro.2016.02.011
7 Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome

Foundation Global Study. Gastroenterology 2021;160:99-114.e3. doi:10.1053/j.gastro.2020.04.014
8 Ghoshal UC, Singh R, Chang F-Y, et al. Epidemiology of Uninvestigated and Functional Dyspepsia in Asia: Facts and Fiction. J Neurogastroenterol Motil 2011;17:235–244. doi:10.5056/jnm.2011.17.3.235
9 Shah SS, Bhatia SJ, Mistry FP. Epidemiology of dyspepsia in the general population in Mumbai. Indian J Gastroenterol 2001;20:103–106.
10 Singh V, Trikha B, Nain CK, Singh K, Vaiphei Kl. Epidemiology of Helicobacter pylori and peptic ulcer in India. J Gastroenterol Hepatol 2002;17:659–665. doi:10.1046/j.1440-1746.2002.02746.x
11 Ghoshal UC, Abraham P, Bhatt C, et al. Epidemiological and clinical profile of irritable bowel syndrome in India: report of the Indian Society of Gastroenterology Task Force. Indian J Gastroenterol 2008;27:22–28.
12 Ghoshal UC, Singh R. Functional dyspepsia: the Indian scenario. J Assoc Physicians India 2012;60 Suppl 6–8.
13 Ford AC, Marwaha A, Sood R, Moayyedi P. Global prevalence of, and risk factors for, uninvestigated dyspepsia: a meta-analysis. Gut 2015;64:1049–1057. doi:10.1136/gutjnl-2014-307843
14 Ford AC, Thabane M, Collins SM, et al. Prevalence of uninvestigated dyspepsia 8 years after a large waterborne outbreak of bacterial dysentery: a cohort study. Gastroenterology 2010;138:1727–1736. doi:10.1053/j.gastro.2010.01.043
15 Pike BL, Porter CK, Sorrell TJ, et al. Acute gastroenteritis and the risk of functional dyspepsia: a systematic review and meta-analysis. Am J Gastroenterol 2013;108:1558–1563. doi:10.1038/ajg.2013.147
16 Oshima T, Fukui H, Watari J, Miwa H. Childhood abuse history is associated with the development of dyspepsia: a population-based survey in Japan. J Gastroenterol 2015;50:744–750. doi:10.1007/s00535-014-1014-3
17 Deding U, Torp-Pedersen C, Bøggild H. Perceived stress as a risk factor for dyspepsia: a register-based cohort study. Eur J Gastroenterol Hepatol 2017;29:560–567. doi:10.1097/MEG.0000000000000831
18 Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of Functional Dyspepsia with Depression and Anxiety: A Systematic Review. J Gastrointestin Liver Dis 2021;30:259-266. doi:10.15403/jgld-3325
19 Sugano K, Tack J, Kuipers EJ, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;64:1353–1367. doi:10.1136/gutjnl-2015-309252
20 Ford AC, Moayyedi P, Jarbol DE, Logan RF, Delaney BC. Meta-analysis: Helicobacter pylori'test and treat' compared with empirical acid suppression for managing dyspepsia. Aliment Pharmacol Ther 2008;28:534–544. doi:10.1111/j.1365-2036.2008.03784.x
21 Mahadeva S, Yadav H, Rampal S, Everett SM, Goh KL. Ethnic variation, epidemiological factors and quality of life impairment associated with dyspepsia in urban Malaysia. Aliment Pharmacol Ther 2010;31:1141–51. doi:10.1111/j.1365-2036.2010.04270.x
22 Talley NJ. Functional dyspepsia: new insights into pathogenesis and therapy. Korean J Intern Med 2016;31:444–456. doi:10.3904/kjim.2016.091
23 Samsom M, Verhagen MA, vanBerge Henegouwen GP, Smout AJ. Abnormal clearance of exogenous acid and increased acid sensitivity of the proximal duodenum in dyspeptic patients. Gastroenterology 1999;116:515–520. doi:10.1016/s0016-5085(99)70171-x
24 Cirillo C, Bessissow T, Desmet AS, Vanheel H, Tack J, Vanden Berghe P. Evidence for neuronal and structural changes in submucous ganglia of patients with functional dyspepsia. Am J Gastroenterol 2015;110:1205–15. doi:10.1038/ajg.2015.158
25 Vanheel H, Vicario M, Vanuytsel T, et al. Impaired duodenal mucosal integrity and low-grade inflammation in functional dyspepsia. Gut 2014;63:262–271. doi:10.1136/gutjnl-2012-303857
26 Walker MM, Aggarwal KR, Shim LS, et al. Duodenal eosinophilia and early satiety in functional dyspepsia: confirmation of a positive association in an Australian cohort. J Gastroenterol Hepatol 2014;29:474–479. doi:10.1111/jgh.12419
27 Aro P, Talley NJ, Ronkainen J, et al. Anxiety is associated with uninvestigated and functional dyspepsia (Rome III criteria) in a Swedish population-based study. Gastroenterology 2009;137:94–100. doi:10.1053/j.gastro.2009.03.039
28 Mak AD, Wu JC, Chan Y, Chan FK, Sung JJ, Lee S. Dyspepsia is strongly associated with major depression and generalised anxiety disorder - a community study. Aliment Pharmacol Ther 2012;36:800–810. doi:10.1111/apt.12036
29 Koloski NA, Jones M, Kalantar J, Weltman M, Zaguirre J, Talley NJ. The brain--gut pathway in functional gastrointestinal disorders is bidirectional: a 12-year prospective population-based study. Gut 2012;61:1284–1290. doi:10.1136/gutjnl-2011-300474
30 Koloski NA, Jones M, Talley NJ. Evidence that independent gut-to-brain and brain-to-gut pathways operate in the irritable bowel syndrome and functional dyspepsia: a 1-year population-based prospective study. Aliment Pharmacol Ther 2016;44:592–600. doi:10.1111/apt.13738
31 Black CJ, Drossman DA, Talley NJ, Ruddy J, Ford AC. Functional gastrointestinal disorders: advances in understanding and management. The Lancet 2020;396:1664–1674. doi:10.1016/S0140-6736(20)32115-2
32 Drossman DA. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology 2016;150:1262-1279.e2. doi:10.1053/j.gastro.2016.02.032
33 Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol 2015;28:203–209.
34 Moayyedi PM, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG Clinical Guideline: Management of Dyspepsia. Am J Gastroenterol 2017;112:988-1013. doi:10.1038/ajg.2017.154
35 Ford AC, Yuan Y, Forman D, Hunt R, Moayyedi P. Helicobacter pylori eradication for the prevention of gastric neoplasia. Cochrane Database Syst Rev 2020;7:CD005583. doi:10.1002/14651858.CD005583.pub3
36 Pinto-Sanchez MI, Yuan Y, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. Cochrane Database Syst Rev 2017;3:CD011194. doi:10.1002/14651858.CD011194.pub2
37 Wang WH, Huang JQ, Zheng GF, et al. Effects of proton-pump inhibitors on functional dyspepsia: a meta-analysis of randomized placebo-controlled trials. Clin Gastroenterol Hepatol 2007;5:178–185. doi:10.1016/j.cgh.2006.09.012
38 Wilhelm SM, Rjater RG, Kale-Pradhan PB. Perils and pitfalls of long-term effects of proton pump inhibitors. Expert Rev Clin Pharmacol 2013;6:443–451. doi:10.1586/17512433.2013.811206
39 Zala AV, Walker MM, Talley NJ. Emerging drugs for functional dyspepsia. Expert Opin Emerg Drugs 2015;20:221–233. doi:10.1517/14728214.2015.1009827
40 Sanaka M, Yamamoto T, Kuyama Y. Effects of proton pump inhibitors on gastric emptying: a systematic review. Dig Dis Sci 2010;55:2431–2440. doi:10.1007/s10620-009-1076-x
41 Quigley EMM. Cisapride: what can we learn from the rise and fall of a prokinetic? J Dig Dis 2011;12:147–156. doi:10.1111/j.1751-2980.2011.00491.x
42 Ford AC, Luthra P, Tack J, Boeckxstaens GE, Moayyedi P, Talley NJ. Efficacy of psychotropic drugs in functional dyspepsia: systematic review and meta-analysis. Gut 2017;66:411–420. doi:10.1136/gutjnl-2015-310721

43 Lahner E, Bellentani S, De Bastiani R, et al. A survey of pharmacological and nonpharmacological treatment of functional gastrointestinal disorders. United European Gastroenterol J 2013;1:385-393. doi:10.1177/2050640613499567

44 Ganguli SC, Cawdron R, Irvine EJ. Alternative medicine use by Canadian ambulatory gastroenterology patients: secular trend or epidemic? Am J Gastroenterol 2004;99:319–326. doi:10.1111/j.1572-0241.2004.04046.x

45 Hu ML, Rayner CK, Wu KL, et al. Effect of ginger on gastric motility and symptoms of functional dyspepsia. World J Gastroenterol 2011;17:105–110. doi:10.3748/wjg.v17.i1.105

46 von Arnim U, Peitz U, Vinson B, Gundermann KJ, Malfertheiner P. STW 5, a phytopharmacon for patients with functional dyspepsia: results of a multicenter, placebo-controlled double-blind study. Am J Gastroenterol 2007;102:1268–1275. doi:10.1111/j.1572-0241.2006.01183.x

47 Suzuki H, Matsuzaki J, Fukushima Y, et al. Randomized clinical trial: rikkunshito in the treatment of functional dyspepsia--a multicenter, double-blind, randomized, placebo-controlled study. Neurogastroenterol Motil 2014;26:950–961. doi:10.1111/nmo.12348

48 Ma TT, Yu SY, Li Y, et al. Randomised clinical trial: an assessment of acupuncture on specific meridian or specific acupoint vs. sham acupuncture for treating functional dyspepsia. Aliment Pharmacol Ther 2012;35:552–561. doi:10.1111/j.1365-2036.2011.04979.x

49 Zeng F, Qin W, Ma T, et al. Influence of acupuncture treatment on cerebral activity in functional dyspepsia patients and its relationship with efficacy. Am J Gastroenterol 2012;107:1236–1247. doi:10.1038/ajg.2012.53

50 Lima FA, Ferreira LE, Pace FH. Acupuncture effectiveness as a complementary therapy in functional dyspepsia patients. Arq Gastroenterol 2013;50:202–207. doi:10.1590/S0004-28032013000200036

51 Calvert EL, Houghton LA, Cooper P, Morris J, Whorwell PJ. Long-term improvement in functional dyspepsia using hypnotherapy. Gastroenterology 2002;123:1778–1785. doi:10.1053/gast.2002.37071

52 Chiarioni G, Vantini I, De Iorio F, Benini L. Prokinetic effect of gut-oriented hypnosis on gastric emptying. Aliment Pharmacol Ther 2006;23:1241–1249. doi:10.1111/j.1365-2036.2006.02881.x

53 Takahashi T. Acupuncture for functional gastrointestinal disorders. J Gastroenterol 2006;41:408–417. doi:10.1007/s00535-006-1773-6

54 Zhou W, Su J, Zhang H. Efficacy and Safety of Acupuncture for the Treatment of Functional Dyspepsia: Meta-Analysis. J Altern Complement Med 2016;22:380–389. doi:10.1089/acm.2014.0400

55 Chiarioni G, Pesce M, Fantin A, Sarnelli G. Complementary and alternative treatment in functional dyspepsia. United European Gastroenterol J 2018;6:5–12. doi:10.1177/2050640617724061

56 Stephens I. Medical Yoga Therapy. Children (Basel) 2017;4:12. doi:10.3390/children4020012

57 Bhavanani AB. YOGA CHIKITSA: Application of Yoga as a THERAPY. 2013. Available from: https://www.academia.edu/34346933/YOGA_CHIKITSA_Application_of_Yoga_as_a_THERAPY (Accessed 18 Nov 2022).

58 International Association Of Yoga Therapists. Definition of Yoga Therapy. 2020. Available from: https://cdn.ymaws.com/www.iayt.org/resource/resmgr/docs_certification_all/2020_updates_scope_ethics/2020-06_defintion_of_yoga_th.pdf (Accessed 15 Feb 2023).

59 Chen KW, Berger CC, Manheimer E, et al. Meditative therapies for reducing anxiety: a systematic review and meta-analysis of randomized controlled trials. Depress Anxiety 2012;29:545–562. doi:10.1002/da.21964

60 Li AW, Goldsmith CAW. The effects of yoga on anxiety and stress. Altern Med Rev 2012;17:21–35.

61 Pascoe MC, Bauer IE. A systematic review of randomised control trials on the effects of yoga on stress measures and mood. J Psychiatr Res 2015;68:270–282. doi:10.1016/j.jpsychires.2015.07.013

62 McCall MC, Ward A, Roberts NW, Heneghan C. Overview of Systematic Reviews: Yoga as a Therapeutic Intervention for Adults with Acute and Chronic Health Conditions. Evid Based Complement Alternat Med 2013;2013:945895. doi:10.1155/2013/945895

63 Sengupta P. Health Impacts of Yoga and Pranayama: A State-of-the-Art Review. Int J Prev Med 2012;3:444–458.

64 Taché Y, Mönnikes H, Bonaz B, Rivier J. Role of CRF in stress-related alterations of gastric and colonic motor function. Ann N Y Acad Sci 1993;697:233–243. doi:10.1111/j.1749-6632.1993.tb49936.x

65 Taché Y, Bonaz B. Corticotropin-releasing factor receptors and stress-related alterations of gut motor function. J Clin Invest 2007;117:33–40. doi:10.1172/JCI30085

66 Enck P, Azpiroz F, Boeckxstaens G, et al. Functional dyspepsia. Nat Rev Dis Primers 2017;3:17081. doi:10.1038/nrdp.2017.81

67 Hausken T, Svebak S, Wilhelmsen I, et al. Low vagal tone and antral dysmotility in patients with functional dyspepsia. Psychosom Med 1993;55:12–22. doi:10.1097/00006842-199301000-00004

68 Balasubramaniam M, Telles S, Doraiswamy PM. Yoga on Our Minds: A Systematic Review of Yoga for Neuropsychiatric Disorders. Front Psychiatry 2013;3:117. doi:10.3389/fpsyt.2012.00117

69 Kavuri V, Selvan P, Malamud A, Raghuram N, Selvan SR. Remedial yoga module remarkably improves symptoms in irritable bowel syndrome patients: A 12-week randomized controlled trial. Eur J Integr Med 2015;7:595–608. doi:10.1016/j.eujim.2015.11.001

70 Streeter CC, Gerbarg PL, Saper RB, Ciraulo DA, Brown RP. Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. Med Hypotheses 2012;78:571–579. doi:10.1016/j.mehy.2012.01.021

71 Innes KE, Bourguignon C, Taylor AG. Risk indices associated with the insulin resistance syndrome, cardiovascular disease, and possible protection with yoga: a systematic review. J Am Board Fam Pract 2005;18:491–519. doi:10.3122/jabfm.18.6.491

72 Bhavanani AB, Raj JB, Ramanathan M, Trakroo M. Effect of Different Pranayamas on Respiratory Sinus Arrhythmia. J Clin Diagn Res 2016;10:CC04-CC06. doi:10.7860/JCDR/2016/16306.7408

73 Khattab K, Khattab AA, Ortak J, Richardt G, Bonnemeier H. Iyengar yoga increases cardiac parasympathetic nervous modulation among healthy yoga practitioners. Evid Based Complement Alternat Med 2007;4:511–517. doi:10.1093/ecam/nem087

74 Raghuraj P, Ramakrishnan AG, Nagendra HR, Telles S. Effect of two selected yogic breathing techniques of heart rate variability. Indian J Physiol Pharmacol 1998;42:467–472.

75 Zhu Y, Xu F, Lu D, et al. Transcutaneous auricular vagal nerve stimulation improves functional dyspepsia by enhancing vagal efferent activity. Am J Physiol Gastrointest Liver Physiol 2021;320:G700–G711. doi:10.1152/ajpgi.00426.2020

76 Lewis MW, Hermann GE, Rogers RC, Travagli RA. In vitro and in vivo analysis of the effects of corticotropin releasing factor on rat dorsal vagal complex. J Physiol 2002;543:135–146. doi:10.1113/jphysiol.2002.019281

77 Taché Y, Larauche M, Yuan P-Q, et al. Brain and Gut CRF Signaling: Biological Actions and Role in the Gastrointestinal Tract. Curr Mol Pharmacol 2018;11:51–71. doi:10.2174/1874467210666170224095741

78 Kamei T, Toriumi Y, Kimura H, et al. Decrease in serum cortisol during yoga exercise is correlated with alpha wave activation. Percept Mot Skills 2000;90:1027–1032. doi:10.2466/pms.2000.90.3.1027
79 Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004;29:448–74. doi:10.1016/s0306-4530(03)00054-4
80 MacLean CR, Walton KG, Wenneberg SR, et al. Effects of the Transcendental Meditation program on adaptive mechanisms: changes in hormone levels and responses to stress after 4 months of practice. Psychoneuroendocrinology 1997;22:277–295. doi:10.1016/s0306-4530(97)00003-6
81 Jevning R, Wilson AF, Davidson JM. Adrenocortical activity during meditation. Horm Behav 1978;10:54–60. doi:10.1016/0018-506x(78)90024-7
82 Cummings DE. Ghrelin and the short- and long-term regulation of appetite and body weight. Physiol Behav 2006;89:71–84. doi:10.1016/j.physbeh.2006.05.022
83 Peeters TL. Central and peripheral mechanisms by which ghrelin regulates gut motility. J Physiol Pharmacol 2003;54 Suppl 4:95–103.
84 Lee KJ, Cha DY, Cheon SJ, Yeo M, Cho SW. Plasma ghrelin levels and their relationship with gastric emptying in patients with dysmotility-like functional dyspepsia. Digestion 2009;80:58–63. doi:10.1159/000215389
85 Shindo T, Futagami S, Hiratsuka T, et al. Comparison of gastric emptying and plasma ghrelin levels in patients with functional dyspepsia and non-erosive reflux disease. Digestion 2009;79:65–72. doi:10.1159/000205740
86 Shinomiya T, Fukunaga M, Akamizu T, et al. Plasma acylated ghrelin levels correlate with subjective symptoms of functional dyspepsia in female patients. Scand J Gastroenterol 2005;40:648–653. doi:10.1080/00365520510015403
87 Akamizu T, Iwakura H, Ariyasu H, Kangawa K. Ghrelin and Functional Dyspepsia. Int J Pept 2010;2010:548457. doi:10.1155/2010/548457
88 Arai M, Matsumura T, Tsuchiya N, et al. Rikkunshito improves the symptoms in patients with functional dyspepsia, accompanied by an increase in the level of plasma ghrelin. Hepatogastroenterology 2012;59:62–66. doi:10.5754/hge11246
89 Yu AP, Ugwu FN, Tam BT, et al. One Year of Yoga Training Alters Ghrelin Axis in Centrally Obese Adults With Metabolic Syndrome. Front Physiol 2018;9:1321. doi:10.3389/fphys.2018.01321
90 Browning KN, Travagli RA. Central Nervous System Control of Gastrointestinal Motility and Secretion and Modulation of Gastrointestinal Functions. Compr Physiol 2014;4:1339–1368. doi:10.1002/cphy.c130055
91 Rogers RC, Hermann GE, Travagli RA. Brainstem pathways responsible for oesophageal control of gastric motility and tone in the rat. J Physiol 1999;514:369–383. doi:10.1111/j.1469-7793.1999.369ae.x
92 Travagli RA, Hermann GE, Browning KN, et al. Brainstem circuits regulating gastric function. Annu Rev Physiol 2006;68:279–305. doi:10.1146/annurev.physiol.68.040504.094635
93 Coulie B, Tack J, Sifrim D, Andrioli A, Janssens J. Role of nitric oxide in fasting gastric fundus tone and in 5-HT1 receptor-mediated relaxation of gastric fundus. Am J Physiol 1999;276:G373-G377. doi:10.1152/ajpgi.1999.276.2.G373
94 Takahashi T. Pathophysiological significance of neuronal nitric oxide synthase in the gastrointestinal tract. J Gastroenterol 2003;38:421–430. doi:10.1007/s00535-003-1094-y
95 Kuiken SD, Vergeer M, Heisterkamp SH, Tytgat GN, Boeckxstaens GE. Role of nitric oxide in gastric motor and sensory functions in healthy subjects. Gut 2002;51:212–218. doi:10.1136/gut.51.2.212
96 Tack J, Demedts I, Meulemans A, Schuurkes J, Janssens J. Role of nitric oxide in the gastric accommodation reflex and in meal induced satiety in humans. Gut 2002;51:219–224. doi:10.1136/gut.51.2.219
97 Bouin M, Lupien F, Riberdy-Poitras M, Poitras P. Tolerance to gastric distension in patients with functional dyspepsia: modulation by a cholinergic and nitrergic method. Eur J Gastroenterol Hepatol 2006;18:63–68. doi:10.1097/00042737-200601000-00011
98 Gilja OH, Hausken T, Bang CJ, Berstad A. Effect of glyceryl trinitrate on gastric accommodation and symptoms in functional dyspepsia. Dig Dis Sci 1997;42:2124–2131. doi:10.1023/a:1018839122354
99 Karthiga K, Pal GK, Dasari P, et al. Effects of yoga on cardiometabolic risks and fetomaternal outcomes are associated with serum nitric oxide in gestational hypertension: a randomized control trial. Sci Rep 2022;12:11732. doi:10.1038/s41598-022-15216-4
100 Udhan VD, Shinde PU, Wankhede SG. Evaluation of Efficacy of Long-term Yogic Training on Vascular Endothelial Function and Cardiovascular Responses in Healthy Individuals. Int J Physiol 2020;8:102–107. doi:10.37506/ijop.v8i3.1338
101 Lakshmanagowda P, Joseph E, Goturu J, et al. Beneficial effect of long term yoga training on serum nitric oxide. Asian J Med Clin Sci 2013;2:44–47.
102 Lee KJ, Kim JH, Cho SW. Dyspeptic symptoms associated with hypersensitivity to gastric distension induced by duodenal acidification. J Gastroenterol Hepatol 2006;21:515–520. doi:10.1111/j.1440-1746.2005.03976.x
103 Lee KJ, Vos R, Janssens J, Tack J. Influence of duodenal acidification on the sensorimotor function of the proximal stomach in humans. Am J Physiol Gastrointest Liver Physiol 2004;286:G278-G284. doi:10.1152/ajpgi.00086.2003
104 Collen MJ, Loebenberg MJ. Basal gastric acid secretion in nonulcer dyspepsia with or without duodenitis. Dig Dis Sci 1989;34:246–250. doi:10.1007/BF01536059
105 Melashchenko S. Assessment of gastric acidity by short-duration intragastric pH-monitoring with standardised breakfast in functional and some other dyspepsias. Prz Gastroenterol 2020;15:258–266. doi:10.5114/pg.2020.99041
106 Gharote ML. Effect of air swallowing on the gastric acidity: A pilot study. Yoga Mimamsa 1971;14:7–10.
107 Malshe PC. Drinking air and maneuvering it to the pyloric region of the stomach for the treatment for Helicobacter pylori infection. Med Hypotheses 2010;75:155–161. doi:10.1016/j.mehy.2010.02.010
108 Geeraerts B, Vandenberghe J, Van Oudenhove L, et al. Influence of experimentally induced anxiety on gastric sensorimotor function in humans. Gastroenterology 2005;129:1437–1444. doi:10.1053/j.gastro.2005.08.020
109 Ly HG, Weltens N, Tack J, Van Oudenhove L. Acute Anxiety and Anxiety Disorders Are Associated With Impaired Gastric Accommodation in Patients With Functional Dyspepsia. Clin Gastroenterol Hepatol 2015;13:1584-1591.e3. doi:10.1016/j.cgh.2015.03.032
110 Holtmann G, Goebell H, Jockenhoevel F, Talley NJ. Altered vagal and intestinal mechanosensory function in chronic unexplained dyspepsia. Gut 1998;42:501–506. doi:10.1136/gut.42.4.501
111 Li M, Xue L, Zhu HY, et al. Protein Kinase C Mediates the Corticosterone-induced Sensitization of Dorsal Root Ganglion Neurons Innervating the Rat Stomach. J Neurogastroenterol Motil 2017;23:464–476. doi:10.5056/jnm16161

112 Lee KJ, Tack J. Duodenal Implications in the Pathophysiology of Functional Dyspepsia. J Neurogastroenterol Motil 2010;16:251–257. doi:10.5056/jnm.2010.16.3.251

113 Vandenberghe J, Dupont P, Van Oudenhove L, et al. Regional cerebral blood flow during gastric balloon distention in functional dyspepsia. Gastroenterology 2007;132:1684–1693. doi:10.1053/j.gastro.2007.03.037

114 Kirchner A, Birklein F, Stefan H, Handwerker HO. Left vagus nerve stimulation suppresses experimentally induced pain. Neurology 2000;55:1167–1171. doi:10.1212/wnl.55.8.1167

115 Ren K, Randich A, Gebhart GF. Effects of electrical stimulation of vagal afferents on spinothalamic tract cells in the rat. Pain 1991;44:311–319. doi:10.1016/0304-3959(91)90102-4

116 Hjelland IE, Svebak S, Berstad A, Flatabø G, Hausken T. Breathing exercises with vagal biofeedback may benefit patients with functional dyspepsia. Scand J Gastroenterol 2007;42:1054–1062. doi:10.1080/00365520701259208

117 Enna SJ, McCarson KE. The role of GABA in the mediation and perception of pain. Adv Pharmacol 2006;54:1–27. doi:10.1016/s1054-3589(06)54001-3

118 Neto FL, Ferreira-Gomes J, Castro-Lopes JM. Distribution of GABA receptors in the thalamus and their involvement in nociception. Adv Pharmacol 2006;54:29–51. doi:10.1016/s1054-3589(06)54002-5

119 Mak ADP, Ho YM, Leung ONW, et al. Unaltered Brain GABA Concentrations and Resting fMRI Activity in Functional Dyspepsia With and Without Comorbid Depression. Front Psychiatry 2020;11:549749. doi:10.3389/fpsyt.2020.549749

120 Liu LS, Shenoy M, Pasricha PJ. The analgesic effects of the GABAB receptor agonist, baclofen, in a rodent model of functional dyspepsia. Neurogastroenterol Motil 2011;23:356-e161. doi:10.1111/j.1365-2982.2010.01649.x

121 Shafigh-Ardestani MH, Karami-Horestani M, Emami B, Arjmandpour A. Evaluating the Effect of Oral Gabapentin on the Improvement of Gastrointestinal Symptoms in Patients with Functional Dyspepsia Resistant to Conventional Treatments. Adv Biomed Res 2019;8:53. doi:10.4103/abr.abr_234_18

122 Mody I, Maguire J. The reciprocal regulation of stress hormones and GABA(A) receptors. Front Cell Neurosci 2011;6:4. doi:10.3389/fncel.2012.00004

123 Streeter CC, Jensen JE, Perlmutter RM, et al. Yoga Asana sessions increase brain GABA levels: a pilot study. J Altern Complement Med 2007;13:419–426. doi:10.1089/acm.2007.6338

124 Streeter CC, Whitfield TH, Owen L, et al. Effects of yoga versus walking on mood, anxiety, and brain GABA levels: a randomized controlled MRS study. J Altern Complement Med 2010;16:1145–1152. doi:10.1089/acm.2010.0007

125 Streeter CC, Gerbarg PL, Brown RP, et al. Thalamic Gamma Aminobutyric Acid Level Changes in Major Depressive Disorder After a 12-Week Iyengar Yoga and Coherent Breathing Intervention. J Altern Complement Med 2020;26:190-197. doi:10.1089/acm.2019.0234

126 Liebregts T, Adam B, Bredack C, et al. Small bowel homing T cells are associated with symptoms and delayed gastric emptying in functional dyspepsia. Am J Gastroenterol 2011;106:1089–1098. doi:10.1038/ajg.2010.512

127 Morgan N, Irwin MR, Chung M, Wang C. The Effects of Mind-Body Therapies on the Immune System: Meta-Analysis. PLoS One 2014;9:e100903. doi:10.1371/journal.pone.0100903

128 Djalilova DM, Schulz PS, Berger AM, Case AJ, Kupzyk KA, Ross AC. Impact of Yoga on Inflammatory Biomarkers: A Systematic Review. Biol Res Nurs 2019;21:198–209. doi:10.1177/1099800418820162

129 Estevao C. The role of yoga in inflammatory markers. Brain Behav Immun Health 2022;20:100421. doi:10.1016/j.bbih.2022.100421

130 Kiecolt-Glaser JK, Bennett JM, Andridge R, et al. Yoga's impact on inflammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial. J Clin Oncol 2014;32:1040–1049. doi:10.1200/JCO.2013.51.8860

131 Yadav RK, Magan D, Mehta N, Sharma R, Mahapatra SC. Efficacy of a short-term yoga-based lifestyle intervention in reducing stress and inflammation: preliminary results. J Altern Complement Med 2012;18:662–667. doi:10.1089/acm.2011.0265

132 Kaliman P, Álvarez-López MJ, Cosín-Tomás M, Rosenkranz MA, Lutz A, Davidson RJ. Rapid changes in histone deacetylases and inflammatory gene expression in expert meditators. Psychoneuroendocrinology 2014;40:96–107. doi:10.1016/j.psyneuen.2013.11.004

133 Twal WO, Wahlquist AE, Balasubramanian S. Yogic breathing when compared to attention control reduces the levels of pro-inflammatory biomarkers in saliva: a pilot randomized controlled trial. BMC Complement Altern Med 2016;16:294. doi:10.1186/s12906-016-1286-7

134 Bower JE, Irwin MR. Mind-body therapies and control of inflammatory biology: A descriptive review. Brain Behav Immun 2016;51:1–11. doi:10.1016/j.bbi.2015.06.012

135 Bower JE, Greendale G, Crosswell AD, et al. Yoga reduces inflammatory signaling in fatigued breast cancer survivors: a randomized controlled trial. Psychoneuroendocrinology 2014;43:20–29. doi:10.1016/j.psyneuen.2014.01.019

136 Black DS, Cole SW, Irwin MR, et al. Yogic meditation reverses NF-κB and IRF-related transcriptome dynamics in leukocytes of family dementia caregivers in a randomized controlled trial. Psychoneuroendocrinology 2013;38:348–355. doi:10.1016/j.psyneuen.2012.06.011

137 Tracey KJ. Reflex control of immunity. Nat Rev Immunol 2009;9:418–428. doi:10.1038/nri2566

138 Pavlov VA, Tracey KJ. The cholinergic anti-inflammatory pathway. Brain Behav Immun 2005;19:493–499. doi:10.1016/j.bbi.2005.03.015

139 Vanuytsel T, van Wanrooy S, Vanheel H, et al. Psychological stress and corticotropin-releasing hormone increase intestinal permeability in humans by a mast cell-dependent mechanism. Gut 2014;63:1293–1299. doi:10.1136/gutjnl-2013-305690

140 Bhole MV. Gastric tone as influenced by mental states and meditation. Yoga Mimamsa 1983;22:54–58.

141 Witte AB, D'Amato M, Poulsen SS, et al. Duodenal epithelial transport in functional dyspepsia: Role of serotonin. World J Gastrointest Pathophysiol 2013;4:28–36. doi:10.4291/wjgp.v4.i2.28

142 Dizdar V, Spiller R, Singh G, et al. Relative importance of abnormalities of CCK and 5-HT (serotonin) in Giardia-induced post-infectious irritable bowel syndrome and functional dyspepsia. Aliment Pharmacol Ther 2010;31:883–891. doi:10.1111/j.1365-2036.2010.04251.x

143 Lee M, Moon W, Kim J. Effect of yoga on pain, brain-derived neurotrophic factor, and serotonin in premenopausal women with chronic low back pain. Evid Based Complement Alternat Med 2014;2014:203173. doi:10.1155/2014/203173

144 Lim SA, Cheong KJ. Regular Yoga Practice Improves Antioxidant Status, Immune Function, and Stress Hormone Releases in Young Healthy People: A Randomized, Double-Blind, Controlled Pilot Study. J Altern Complement Med 2015;21:530–538. doi:10.1089/acm.2014.0044

145 Devi SK, Chansauria JP, Udupa KN. Mental depression and kundalini yoga. Anc Sci Life 1986;6:112–118.

146 Nirwan M, Halder K, Saha M, Pathak A, Balakrishnan R, Ganju L. Improvement in resilience and stress-related blood markers following

ten months yoga practice in Antarctica. J Complement Integr Med 2020;18:201–207. doi:10.1515/jcim-2019-0240

147 Brown RP, Gerbarg PL. Sudarshan Kriya yogic breathing in the treatment of stress, anxiety, and depression: part I-neurophysiologic model. J Altern Complement Med 2005;11:189–201. doi:10.1089/acm.2005.11.189

148 Cramer H, Lauche R, Anheyer D, et al. Yoga for anxiety: A systematic review and meta-analysis of randomized controlled trials. Depress Anxiety 2018;35:830–843. doi:10.1002/da.22762

149 Kirkwood G, Rampes H, Tuffrey V, Richardson J, Pilkington K. Yoga for anxiety: a systematic review of the research evidence. Br J Sports Med 2005;39:884–891. doi:10.1136/bjsm.2005.018069

150 Rod K. Observing the Effects of Mindfulness-Based Meditation on Anxiety and Depression in Chronic Pain Patients. Psychiatr Danub 2015;27 Suppl 1:S209-S211.

151 Mizrahi MC, Reicher-Atir R, Levy S, et al. Effects of guided imagery with relaxation training on anxiety and quality of life among patients with inflammatory bowel disease. Psychol Health 2012;27:1463–1479. doi:10.1080/08870446.2012.691169

152 Gerbarg PL, Jacob VE, Stevens L, et al. The Effect of Breathing, Movement, and Meditation on Psychological and Physical Symptoms and Inflammatory Biomarkers in Inflammatory Bowel Disease: A Randomized Controlled Trial. Inflamm Bowel Dis 2015;21:2886–2896. doi:10.1097/MIB.0000000000000568

153 Sharma VK, Trakroo M, Subramaniam V, Rajajeyakumar M, Bhavanani AB, Sahai A. Effect of fast and slow pranayama on perceived stress and cardiovascular parameters in young health-care students. Int J Yoga 2013;6:104–110. doi:10.4103/0973-6131.113400

154 Kreibig SD. Autonomic nervous system activity in emotion: a review. Biol Psychol 2010;84:394–421. doi:10.1016/j.biopsycho.2010.03.010

155 Breit S, Kupferberg A, Rogler G, Hasler G. Vagus Nerve as Modulator of the Brain–Gut Axis in Psychiatric and Inflammatory Disorders. Front Psychiatry 2018;9:44. doi:10.3389/fpsyt.2018.00044

156 Pilkington K, Kirkwood G, Rampes H, Richardson J. Yoga for depression: the research evidence. J Affect Disord 2005;89:13–24. doi:10.1016/j.jad.2005.08.013

157 Ramanathan M, Bhavanani AB, Trakroo M. Effect of a 12-week yoga therapy program on mental health status in elderly women inmates of a hospice. Int J Yoga 2017;10:24–28. doi:10.4103/0973-6131.186156

158 Woolery A, Myers H, Sternlieb B, Zeltzer L. A yoga intervention for young adults with elevated symptoms of depression. Altern Ther Health Med 2004;10:60–63.

159 Kumar S, Subramaniam E, Bhavanani AB, Sarkar S, Balasundaram S. Effect of adjunct yoga therapy in depressive disorders: Findings from a randomized controlled study. Indian J Psychiatry 2019;61:592–597. doi:10.4103/psychiatry.IndianJPsychiatry_173_19

160 Lee IS, Wang H, Chae Y, Preissl H, Enck P. Functional neuroimaging studies in functional dyspepsia patients: a systematic review. Neurogastroenterol Motil 2016;28:793–805. doi:10.1111/nmo.12793

161 Tang YY, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. Nat Rev Neurosci 2015;16:213–225. doi:10.1038/nrn3916

162 Luders E, Toga AW, Lepore N, Gaser C. The underlying anatomical correlates of long-term meditation: Larger hippocampal and frontal volumes of gray matter. Neuroimage 2009;45:672–678. doi:10.1016/j.neuroimage.2008.12.061

163 Jia W, Zhen J, Liu A, et al. Long-Term Vegan Meditation Improved Human Gut Microbiota. Evid Based Complement Alternat Med 2020;2020:9517897. doi:10.1155/2020/9517897

164 Ningthoujam DS, Singh N, Mukherjee S. Possible Roles of Cyclic Meditation in Regulation of the Gut-Brain Axis. Front Psychol 2021;12:768031. doi:10.3389/fpsyg.2021.768031

165 Wilder-Smith CH, Li X, Shen L, Cao Y, Ho KY, Wong RK. Dysfunctional endogenous pain modulation in patients with functional dyspepsia. Neurogastroenterol Motil 2014;26:489–498. doi:10.1111/nmo.12291

166 Kakigi R, Nakata H, Inui K, et al. Intracerebral pain processing in a Yoga Master who claims not to feel pain during meditation. Eur J Pain 2005;9:581–589. doi:10.1016/j.ejpain.2004.12.006

167 Cotton VA, Low LA, Villemure C, Bushnell MC. Unique Autonomic Responses to Pain in Yoga Practitioners. Psychosom Med 2018;80:791–798. doi:10.1097/PSY.0000000000000587

168 Morone NE, Greco CM. Mind-body interventions for chronic pain in older adults: a structured review. Pain Med 2007;8:359–375. doi:10.1111/j.1526-4637.2007.00312.x

169 Cramer H, Lauche R, Langhorst J, Dobos G. Yoga for depression: a systematic review and meta-analysis. Depress Anxiety 2013;30:1068–1083. doi:10.1002/da.22166

170 Lemay V, Hoolahan J, Buchanan A. Impact of a Yoga and Meditation Intervention on Students' Stress and Anxiety Levels. Am J Pharm Educ 2019;83:7001. doi:10.5688/ajpe7001

171 D'Silva A, MacQueen G, Nasser Y, Taylor LM, Vallance JK, Raman M. Yoga as a Therapy for Irritable Bowel Syndrome. Dig Dis Sci 2020;65:2503–2514. doi:10.1007/s10620-019-05989-6

172 Schumann D, Anheyer D, Lauche R, Dobos G, Langhorst J, Cramer H. Effect of Yoga in the Therapy of Irritable Bowel Syndrome: A Systematic Review. Clin Gastroenterol Hepatol 2016;14:1720–1731. doi:10.1016/j.cgh.2016.04.026

173 Taneja I, Deepak KK, Poojary G, Acharya IN, Pandey RM, Sharma MP. Yogic versus conventional treatment in diarrhea-predominant irritable bowel syndrome: a randomized control study. Appl Psychophysiol Biofeedback 2004;29:19–33. doi:10.1023/b:apbi.0000017861.60439.95