


# Retracted: Exploring the microbiome and mindfulness connection

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Mental health and its impact on overall well-being is a topic that is at the forefront of consideration in most industrialized countries. Ironically in the expansive world of the microbiome, gut microbes are most affected by modern, fast paced, westernized lifestyles, indicating a significant correlation based on geography, and physical and mental habits. The gut–brain axis is an established axis demonstrating the effect of the gut microbiota on the biochemical processes in the brain. With the existence of mindfulness initiatives such as adoption of a ‘yogic lifestyle’ aimed at creating a sense of harmony and balance within the individual, this special report considers the available evidence base, asking whether the harmony created by adopting this lifestyle can be related to establishing harmony in the gut–brain axis.

**Lay abstract:** In current times, mental health has been given much significance for the overall health of the individual. The microbiome provides a new gateway to approach mental health through the gut via the established gut–brain axis. This opinion article explores the current evidence establishing the strong gut–brain connection. We discuss the impact of lifestyle, yoga and mindfulness in balancing and creating mental health based on this data.

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Wellness initiatives are starting to take a center stage in most developed countries, with an emphasis being put on mindfulness and mental balance. Activities that bring ‘harmony’ to the mind–body connection are encouraged, given the increasing rates of mental illness such as anxiety, depression and suicide in the population [1–3]. In the last decade, research has begun to focus on creating a scientific basis for how mindfulness activities like yoga and other lifestyle-based approaches can be connected to a healthy physiology. In this article, we explore the impact of mindfulness a step further, and more scientifically, by examining the connection of the gut and brain via the microbiome–host physiology, as discussed in recent scientific literature.

Anatomically, the gut has a unique connection to the brain bidirectionally through neurohumoral pathways that can significantly alter states of homeostasis [4,5].

The gut has a large amount of microflora that are intricately involved in the physiology of gut functioning. The state of ‘symbiosis’ between the microbial flora and host results in healthy physiology and healthy states, and only recently have we begun to unravel that its altered or dysbiotic state can influence mental illness and *vice versa* [6].

## Neurobiology of stress through the brain & gut

In order to establish the physical and chemical pathways connecting the microbiome and neurobiology of anxiety, it is essential to first understand the major neuroendocrine activities that precipitate fear-based behavior [7]. According to J Watson, the father of behaviorism, emotions that trigger behavior are dominated by ‘visceral

and glandular factors' [8]. Research in the past 15 years substantiates that anxiety behaviors and symptoms are predominantly activated through the autonomic nervous system and the hypothalamus–pituitary–adrenal axis [9]. The autonomic nervous system has profound influence over the activity of the intestinal tract, by regulating smooth muscle contractions, pH, motility, mucus secretion and mucosal immune response [9,10]. Both sympathetic and parasympathetic systems dispense cortical and subcortical directives, but the sympathetic system, via the noradrenaline neurotransmitter, is the main promotor of characteristic anxiety symptoms such as alertness, arousal, sweating, hypertension and tachycardia [10,11].

In various observational trials and studies over the past decade, a strong correlation has been placed on autoimmune disorders related to the gut, showing neuroinflammation detected via activation of serum cytokines such as IL-6. Mental illnesses such as anxiety, depression and schizophrenia, and cognitive development disorders such as autism have been linked to gut microbiome dysbiosis [12,13].

### Stress & the microbiome connection

The gut–brain axis (GBA) is a complex bidirectional communicative and regulatory system involving (but not limited to) the brain and central nervous system and the enteric environment of the gut, inclusive of human and microbial cells, metabolites, neuroactive chemicals and energy substrates. The gut and the brain send and receive messages via the enteric nervous system (ENS) through neural pathways such as the efferent sympathetic system and the afferent vagal nerve, as well as through the bloodstream [10,11]. Antibiotics and probiotics have also been considered to influence behavior in mice and humans through the GBA [14,15]. The ENS also innervates the gastrointestinal tract, pancreas and the gall bladder. Thus, the gut and its microbiota affect immunity, endocrine function and the nervous system, as well as regulation of behavior [16]. Therefore, stress and the accompanying arousal affect gastrointestinal function through top-down and bottom-up signals via the ENS [17].

### Signal transduction the brain–gut pathway summarized

- Luminal cells such as enterocyte, enterochromaffin and immune cells of the gut communicate with luminal microbial proteins and via metabolites and neuropeptides [18].
- The concept of a 'leaky gut' theorises that the microbial lipoproteins and polysaccharides are released into the circulation of the host via epithelial cell tight junctions triggering a host immune response [19].
- The adrenergic and noradrenaline pathway efferent nerves release signals into the gut lumen during traumatic or stressful times [20].
- Signaling via adrenergic homologs that cross-activate bacterial and host adrenergic receptors [21].
- The sympathetic nervous system, in states of anxiety and fear, has a restrictive action on the gut, and is able to halt intestinal motor function and fluid secretion, which restricts lumen motility and alters microbial activity such as gene expression and metabolite production [22]. Therefore, states of anxiety or fear that increase sympathetic fight-or-flight shift microbial composition in favor of opportunistic pathogens [23].
- The metabolites of microbial species can influence the enteric and systemic health in both a pro- and anti-inflammatory state and can be found in the bloodstream, which indicates increased permeability of the gut in these states [25,26].
- Microbial-derived toxins like 4EPS and cresol are found to be related to autism, and recently to inhibit myelin gene expression. This shows a correlation of the microbiome to neuroplasticity and early as well as long-term brain development [27,28], implicating the microbiome in early developmental and long-term plasticity that directly affects stress tolerance and resilience.
- Research with probiotics has shown a strong correlation to the states of anxiety and depression; *Lactobacillus* and *Bifidobacterium* are found to exert a profound anxiolytic influence through the production of GABA, 5-HT and short chain fatty acids (SCFAs), and by dampening hypothalamus–pituitary–adrenal adrenergic reaction [24,29].

### Nutrition & its impact on the microbiome & mental state

In ancient times, that is, thousands of years prior to documented scientific literature, most holistic schools of thought including Ayurveda believed that 'you are what you eat'; this is similar to what Hippocrates stated: "*All health begins in the gut*".

We can see in the above-cited literature that there is most definitely a significant communication between the gut, the gut microbes and the brain and overall mental state. Therefore, one can appreciate the importance of nutrition in this equation. A number of human studies and meta-analyses of dietary treatment approaches show

connections in several aspects of mental health, mental disorders and cognition: a relationship between diet and depression in children [30]; a connection between an unhealthy prenatal diet with later acting out behavioral problems in preschool children [31]; and an association between ‘junk food’ and cognitive impairment [32]. There is fairly consistent agreement that diets should include a balance of organic fruits, vegetables, whole grains, fish rich in omega-3 fatty acids and healthy oils like those from olives and nuts (e.g., the Mediterranean diet) [31]. Critically, diets that are diverse with regard to the types of polysaccharides (complex carbohydrates) are considered essential for feeding the microbiota, promoting long-term symbiosis with high diversity populations and upregulating the metabolic output of both primary and secondary (i.e., crossfeeding or cometabolizers) metabolism [26,27,32]. Research in the field of probiotics looking into mode of action and/or side effects promises more therapeutics options. Further studies are warranted to establish how prebiotic and probiotic interventions may help to balance brain function in healthy and diseased individuals [32].

The co-relation of weight, metabolism and inflammatory process in diabetics was studied in patients taking a plant based diet for 24 months by Medawar *et al.* in 2019. Their study concluded an improvement in these markers and proposed novel microbiome-related pathways through which plant-based diets can modulate the microbiome [33]. A recent study published in 2019 by Daneshzad *et al.*, sought to compare plant-based dietary index and dietary acid load with sleep status as well as mental health in Type 2 diabetic women [34]. The study concluded that participants with higher dietary acid load scores and patients who adhered to animal-based rather than plant-based diets were more likely to be poor sleepers and have mental health disorders.

A study conducted by Zhang *et al.* and published in 2018 studied the impact of a 3-month vegetarian diet on gut microbiota and immune repertoire. They found that a number of bacterial species that are associated with the expression level of IgA (a protective immunoglobulin for the gut), a lower diversity of T-cell repertoire and expression level of IgE, as well as a reduced abundance of inflammation-related genes in the gut microbiota were potentially associated with a control group with long-term vegetarians [35]. Thus, they concluded that composition and duration of the diet may have an impact on the balance of pro-/anti-inflammatory factors in the gut microbiota and immune system.

Further to this, a review published in 2019 by Yang *et al.* discussed some new clinical randomized controlled trials examining the impact of nutrition, including diets or prebiotics, with their impact on the gut microbiota and anxiety or irritable bowled syndrome (IBS). More than half of the studies included showed it was positive to treat anxiety symptoms by regulation of intestinal microbiota. They also highlighted that the nonprobiotic interventions were more effective than the probiotic interventions [36].

## A positive mind–body connection through a lifestyle approach

In the western world, there has been a notable push toward adopting an eastern way of life as a means to creating mental harmony, resulting in an increase in wellness and the ‘yoga lifestyle’ movement [37]. The concept of yoga is based on creating harmony of the mind, body and spirit. The definition is achieving a state of ‘union’ of the individual self with the universal consciousness and thereby creating harmony in oneself. According to ancient yogic text, the Yoga Sutras of Patanjali, there are eight paths in which one can attain the union and balance of the mind and spirit. These include yama and niyamas, which are based on restraints and observances of a yogi that create a mode of conduct to balance day-to-day life in mindfulness and lifestyle. Emphasis is placed on conducts that bring purity of thought and ahimsa (nonviolence); for many this includes adopting a vegan/plant-based/vegetarian or meatless diet. The other paths include asana (physical practice of yoga), dhyana (meditation) and pranayama, a breathing technique.

There is a reasonable evidence base supporting the improvement of superoxide dismutase, cytokines, interleukins and other immune modulatory markers when adopting specific yoga poses and breathing techniques, as well as lifestyles [36]. Mindfulness exercises that include breathing and visualizations as well as positive mind–body connections based on intention and affirmations have been demonstrated to reduce burdens of work-related stress and anxiety, and improve self-image [38].

The emotional body has been connected to the endocannabinoid and neurohumoral pathways of stress reception and stress response [43]. The different techniques of Tantra Yoga that use visualization to balance energy centers help balance corresponding endocrine glands related to those energy centers [37–39].

In 2019, D’Silva *et al.* published a comprehensive review of multiple trials looking at the impact of yoga on IBS [40]. Certain data from randomized controlled studies found yoga to be more effective compared with

pharmacology-based therapies and equally effective as dietary interventions. These preliminary data support yoga as beneficial in populations dealing with IBS, dysmotility, depression and gastrointestinal-related specific anxiety [40].

### Future perspective

Overall, there is growing evidence in support of the positive benefits of yoga and yogic lifestyles on the overall health and harmony of an individual – both mentally and emotionally – in order for them to gain stability and daily adaptability. The advancement of research in this complementary field requires further understanding of the connection between the microbiota and the mind–body and how they are affected by yogic practices and lifestyles. At this time, there is enough evidence to support that there is much to be explored in this field; we have only touched the surface. Understanding the GBA will undoubtedly help us understand how we as individuals are influenced by external and internal forces – forces that are greater than what we once simply considered – that of either a diseased or a healthy state [42]. The microbiome encourages us to look closer at the impact of the ‘environment’ and ‘lifestyle’, to have a more comprehensive approach to creating a healthy state [43]. Once considered complementary and alternative, the practice of yogic breathing, exercise and lifestyle could quite possibly influence not just the mind but also the microbiome. More research is needed to determine the changes in the microbial flora and mental health once such a lifestyle is adopted. One of the biggest limitations in these types of studies is the confounding effect of various aspects of a lifestyle change. However, with more participation and larger scale trials we should be able to accrue a clearer understanding of the benefits.

#### Executive summary

##### The current importance of wellness initiatives supporting mental health

- The recent decade has put a lot of emphasis on mental illness and anxiety in the collective population due to various factors.
- Microbiome–gut–brain research has shown a correlation to this condition.

##### Neurobiology of stress

- The pathways of stress are intricate and span the brain as well as the body in anatomical, physiological and biochemical ways.

##### Gut–brain connection

- The published data that expand our knowledge on the influence the gut–brain connection suggest it can have an impact on mental health.

##### Impact of nutrition on mental health

- This topic needs further exploration but based on recent research promises a new paradigm to manage mental health.

##### Yoga lifestyle & mindfulness & its impact on mental health

- Improving our understanding of ancient approaches could help our current day crisis of mental illness.

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