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Stress as a Topic of Concern in Gut Health: A Review

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

When stress overwhelms the body or persists for a long time (chronic stress), the body is affected by it in a number of ways. Stressors can trigger a variety of stress reactions, including psychological, physiological, and behavioural ones. A multitude of health problems that impact most of the body's systems are brought on by prolonged exposure to such stress. Both physical and mental health is impacted by stress. Perhaps not everyone's bodies react to stress in the same way. Depending on the person's genotype, sex, age, physiological conditions, and prior experiences, it might be different. However, some of these effects apply to everyone. Additionally, stress may work in conjunction with other pathogenic factors to induce gastrointestinal illness. Higher amounts of corticoids and adrenaline are primarily responsible for the effects. Disrupted eating habits, acid reflux, diarrhoea, or constipation are common indications of stress. Stress should be managed by making tiny changes to attitude and way of life, even though it is impossible to escape stress in day-to-day existence.

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1. INTRODUCTION

No Human being is an exception to the susceptibility of the universal anthropogenic condition known as stress. Stress can be physical as well as psychological. Challenges, threats, or concerns about unfavourable past, present and future events can all cause psychological stress. Stress of this kind triggers the brain's stress response mechanisms, which then have an impact on the body. Stress affects several of the body's major systems, including the cardiovascular, muscular, urinary, gastrointestinal, and sweat glands, frequently with negative results. Stress is a harmful or potentially dangerous response of the body that is triggered by damaging external factors [1]. The relationship between social psychology and biological behaviours and tumorigenesis has been extensively studied.

Two facets of GI function can be used to sum up the impact of stress on nutrition and the gastrointestinal (GI) system. First, stress can affect appetite [2-4]. Stress may reduce the amount of blood and oxygen reaching the stomach, which could result in cramps, inflammation, or a bacterial imbalance in the gut. Additionally, it may worsen main gastrointestinal conditions like Irritable bowel syndrome (IBS), Inflammatory bowel disease (IBD), peptic ulcers, gastroesophageal reflux disease (GERD). Stress can cause and exacerbate gastrointestinal discomfort and other symptoms complicating the link between environmental or psychological stress and gastrointestinal distress.

2. FUNCTIONAL PHYSIOLOGY

According to Kiliaan et al. [5] stress can also change the functional physiology of the intestine. Stress is linked to a number of inflammatory diseases, including Crohn's disease and other GI ulcerative diseases [6]. Even early-life stress may contribute to chronic disorders as adults, according to some research [7]. The condition known as irritable bowel syndrome has an inflammatory component origin, is highly related to stress [8].

The autonomic nervous system controls vital processes like breathing, heartbeat, blood pressure, and body temperature. There are two main divisions in this intricate neural network, which runs from the brain to all of the body's major organs. The "fight or flight" reaction is set off by the sympathetic nervous system later the body is calmed by the parasympathetic nervous system. The enteric nervous system, a less well-known part of the autonomic nervous system that aids in digestion regulation, interacts with both the sympathetic and parasympathetic nervous systems. The brain and gut are connected by a number of parallel pathways, collectively known as the brain-gut axis (BGA), including the autonomic nervous system (ANS), the hypothalamus pituitary-adrenal axis (HPA), and other connections [9,10]. In the context of the emergence of various gut illnesses, the interaction of the immune system, brain-gut axis, and gut microbiota is crucial in regulating the gut's stress response [11].

3. ROLE OF NEUROTRANSMITTERS

As it uses the same kinds of neurons and neurotransmitters as the central nervous system (brain and spinal cord), the enteric nervous system is sometimes referred to as a "second brain." With more than 100 million nerve cells buried in the lining of the gastrointestinal tract from the oesophagus to the anus, the enteric nervous system regulates swallowing, secreting enzymes to break down food, assimilation of nutrients, and excretion of waste materials. Neurons lining the digestive system detect when food has entered the gut and send a signal to muscle cells to start a sequence of intestinal contractions that move the meal forward and break it down into nutrients and trash. Neurotransmitters like serotonin are used by the enteric nervous system to connect and communicate with the central nervous system at the same time. Seratonin contributes to the feeling of vigour and enthusiasm. Interestingly, the gut is where a significant amount of serotonin is produced. Therefore, lowering serotonin levels can lead to depression and neurological issues in addition to disrupting bowel movements and causing constipation, endangering the health of the brain.

The body's sympathetic nervous system, which controls autonomic nervous system components including blood pressure, heart rate, and breathing, secretes the stress hormone cortisol in response to stress. Constipation, diarrhoea, and exacerbations of reflux are all brought on by cortisol. This hormone can cause conditions like irritable bowel syndrome, intestinal inflammation,

and stomach ulcers upon continuous and persistent secretion.

Studies have shown that stress affects the absorption process, intestinal permeability, mucus and stomach acid secretion, function of ion channels, and GI inflammation [12,13]. Stress also increases the response of the GI system to inflammation and may reactivate previous inflammation and accelerate the inflammation process by secretion of mediators such as substance P [12]. Stress, anxiety, depressive symptoms, and social behaviour are all significantly influenced by the gut microbiota on the brain. There are a number of pathways, such as neuronal, immunological, and endocrine signals, that may mediate this microbiome-gut-brain axis [14].

4. STRESS AND THE TONGUE

Geographic Tongue (GT) is a benign inflammatory condition with an unidentified aetiology that is characterised by epithelium loss brought on by the atrophy of filiform papillae. The dorsum of the tongue is often where it develops, though it can also reach the lateral borders. It presents as an erythematous patch with pale, somewhat raised edges. Although many people with the illness experience no symptoms, some people may experience tongue burning [15]. In addition to being frequently observed in people with immunological illnesses like psoriasis, stress and/or anxiety, allergy or atopic problems, GT has also been recorded in patients with a family history of the same ailment [16]. A psychological influence has a significant impact on the oral mucosa's reactivity. When emotions or conflicts are expressed directly through oral disorders, as is sometimes the case, lesions of the mouth may be an indirect sign of an emotional issue [17,18]. RAS has already been linked to psychological stress, which is a known RAS trigger that is frequently seen during stressful situations, including test times and major life transitions [19,20].

5. STRESS AND THE STOMACH

Infection with Helicobacter pylori and misuse of NSAIDs (non-steroidal anti-inflammatory medicines) are the two most significant causes of ulcers. Stress, however, can also cause sickness in addition to these other variables. Stress can alter the way that gastric acid is secreted, as well as the amount of HCO_3 that shields the gastric mucosa from hydrochloric acid and the blood flow to the mucosa. Additionally, it might hinder mucosa renewal and negatively impact stomach motility [21].

6. STRESS AND THE OESOPHAGUS

Stress has profound affects on both physical and emotional well-being. Due to the long-term effects of acid on the stomach and oesophagus, the relationship between stress and acid reflux can potentially have a number of negative health repercussions. These consist of oesophageal, gastric, and intestinal ulcers, Barrett's oesophagus, which can lead to esophageal cancer, and gastrointestinal bleeding from ulcers, which, in extreme situations, can be fatal. Despite their frightening sound, these issues may typically be prevented with self-care. Knowing whether stress is having an impact on mental and physical health is crucial. The primary signs and symptoms of gastro-oesophageal reflux disease (GERD) include heartburn and acid regurgitation, which are brought on by the reflux of gastric acid into the oesophagus. Additionally, it may exhibit belching, nausea, nonobstructive dysphagia, or chest pain owing to GERD.

Functional oesophageal disorders include functional chest pain, functional heartburn, reflux hypersensitivity, globus, and functional dysphagia [22]. Yamasaki et al. [23] showed that CRH injection increased esophageal electrical sensitivity in healthy subjects, highlighting the critical role of stress in esophageal sensitivity. A crucial modulator of the gut stress response, peripheral CRH has been demonstrated to have an impact on human visceral hypersensitivity [24].

7. STRESS AND THE INTESTINE

Ingested food, local bacteria, invasive viruses, and other antigens constantly expose the gut mucosa to a massive load of them. A key role in nutritional digestion and absorption is played by the single-cell epithelial layer that lines the gut lumen, which has a surface area of around $300m^2$. At the same time, this layer also serves as the organism's primary barrier between its internal and external environments. In a healthy state, the epithelium only permits trace amounts of intact antigens to penetrate the mucosa, where they interact with the mucosal immune system to reduce inflammation (a process known as oral tolerance). However, in order to start the inflammatory response needed to eliminate the infection, enteric pathogens must stimulate

immune cells. Excessive antigen penetration through the epithelial layer may cause inappropriate immune stimulation and chronic gastrointestinal inflammation in various illness situations, such as inflammatory bowel disease.

By secreting fluid and mucus into the lumen together with secretory IgA to dilute, wash away, and bind harmful compounds, intestinal epithelium exerts a significant physiological defense. Both Crohn's disease and food allergies have been linked to a disruption in intestinal barrier function. Increased mucosal permeability is linked to the pathogenesis and progression of a number of different disease conditions, including stress, ulcerative colitis, multiple organ dysfunction syndrome, and viral and bacterial gastroenteritis. In "leaky gut syndrome", it is thought that the absorption of numerous toxic compounds from the gut lumen causes a variety of problems, although only a few of these statements are supported by convincing scientific data.

Due to the strict regulation of intestinal barrier homeostasis, intestinal hyperpermeability and inflammation may result from a malfunction in the microbiota's composition. Inflammation of the digestive tract can increase intestinal permeability and promote pathobiont colonisation of the microbiota. It is challenging to determine each factor's function as a cause or effect in complicated, well-established illnesses since intestinal permeability, microbiota, and immune response interact with one another [25,26]. Increased intestinal inflammation and altered intestinal motility are caused by stress-induced alterations to the microbiome [27]. Recent research indicates that stress affects not just the microbiota-gut-brain axis but also the neuroendocrine and neuroimmune axes, offering a method by which stress may "get into the belly" to increase health risk [28].

8. IBD AND IBS

Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) are two gastrointestinal illnesses that are influenced by stress. IBS is a highly fascinating model to investigate how stress affects the intestinal barrier. Strong data suggests that people with IBS have higher emotional response to psychological stress, such as the Stroop, dichotomous listening, mental arithmetic task, TSST, critical anger stressor, and public speaking [29]. In fact, the occurrence of stressful situations is thought to contribute to the development and/or maintenance of IBS [30,31]. Having a healthy sleep pattern, which includes an early chronotype, sleeping 7-9 hours per day, never or rarely experiencing insomnia, not snoring, and not frequently experiencing excessive daytime sleepiness, was linked to a significantly lower risk of IBS, regardless of a person's genetic susceptibility to the condition. This association was also partially mediated by mental health scores. Additionally, neuroticism and signs of psychological distress were linked to a lower likelihood of developing IBS [32]. FD, IBS, and reflux esophagitis were linked to stress and sadness. Peptic ulcer illness, colon and stomach adenoma/carcinoma, and depression have all been connected [33]. The six different actions that stress has on the GI system are gut permeability is altered, GI tract movement abnormalities, increased visceral irritation, altered rates and amounts of various GI secretions, detrimental effects on blood flow to the GI tract, and elevated gut bacteria counts are some of the symptoms [34].

9. CONCLUSION

Stress that lasts for a long time or is "chronic" might harm the health permanently. Stress can modify the gut flora, which can impact how the body controls fats and immunological defenses, though the connection between the two is currently unclear. These alterations lead to the development of the metabolic syndrome, a cluster of illnesses that includes obesity, Type 2 diabetes, hyperlipidemia, fatty liver disease, coronary artery disease, high blood pressure, and an inflammatory state. Real digestive disorders like peptic ulcer disease (PUD), irritable bowel syndrome (IBS), and gastroesophageal reflux disease (GERD) can all be brought on by stress.

Treatment of intestinal distress is complicated due to the interaction between the psychological causes of stress and the physiological diseases that may arise. Psychological therapies are frequently combined with medical therapies. These could consist of hypnosis, cognitive behavioural therapy, psychotherapy, or anti-anxiety drugs. It is generally recognised that stress can harm the intestinal barrier permanently. It would be very interesting to conduct cross-disciplinary research on stress, intestinal barrier function, and autoimmune diseases in order to get fresh insight into the pathophysiology of these conditions.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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