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It's all in the noise: A review of noise stress on gastric secretions via the stimulation of corticosteroids and management options

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Abstract

One of the toughest sources of restrictions on the environment and the workplace is noise. Numerous impacts of noise on the immune system, hormone levels, and the cardiovascular and pulmonary systems have been well recognized. In this regard, noise induced stress imparts a very serious effect on the body and is considered one of the richest elements of pollution in the environment. It is well documented in the research arena that noise affects immune function, hormonal levels, and the cardiovascular and respiratory systems through the secretion of hormones and other biomolecules. For example, the excessive secretion of acids leads to an acidic bounce or the peptic juice over secretion that can end with gastric as well as the peptic ulcers. This review article was focused on the latest information concerning gastric acid secretion through noise induced corticosteroid hormones. The pathophysiology of noise stress-induced disorders is heavily influenced by the disruption of the brain-gut axis. Noise stress enhances visceral sensitivity, affects gastrointestinal (GI) motility, increases intestinal permeability, and profoundly activates mast cells, which release a variety of proinflammatory mediators. The main aim here is to make clear that the effects of noise of varying intensities can alter gastric stimulation and key health issues so that the medical community can focus on probable treatment options, something that has not been acknowledged in medicine to date.

Keywords: animal models, corticosteroids, gastric secretion, noise, therapeutics

1. Introduction

Continuous exposure to noise, mostly hard noise, affects human health based on its sequence of origin, which mostly depends on noise frequency, time of noise exposure during the day, and noise exposure duration. Further noise sensitivity and prior exposure are important factors to be considered.

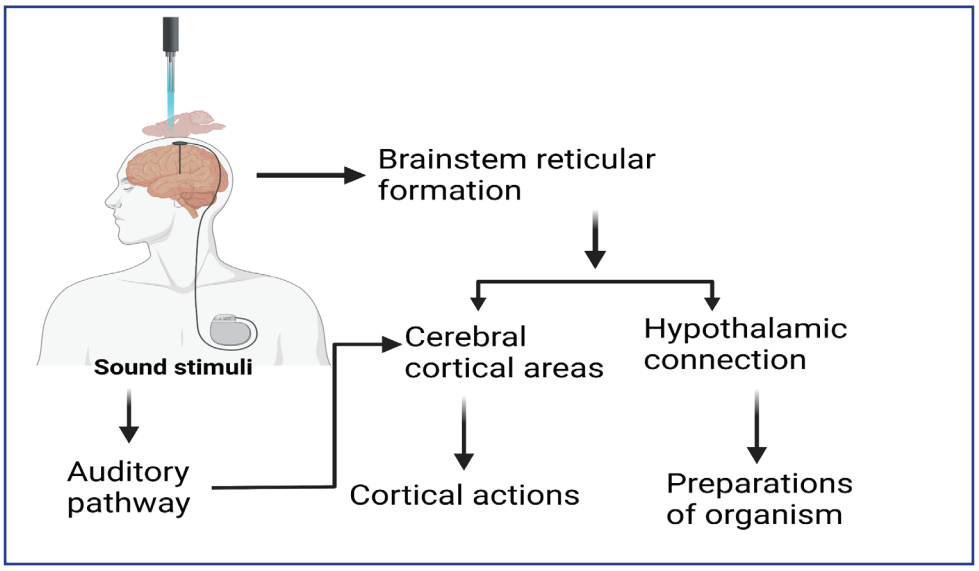

Figure 1. Probable pathophysiological mechanisms of noise effects

Figure 1 describes the pathophysiological mechanisms that initiate sound stimuli, which clearly indicate the acute as well as the chronic effects of noise [1]. An acute response of noise can be different for different organs; it majorly affects the heart rate, blood pressure, respiratory frequency, gastric secretion and motility through the various physiological changes in the body like adrenal hormone secretion, etc. Peripheral vasoconstriction and delayed responses are due to the expected stimuli, persistence of stimulus, and strength of sound levels [2-3]. The response and the stimulus depend on the duration of exposure, as the short term will have its own response compared to the long term. With respect to the exposure, various other factors can influence the effects of noise like sound pressure, exposure, time and frequency of the noise [4]. Infrasonic and ultrasonic waves, as well as tone components, make up noise spectrum characteristics.

The central and peripheral neurological systems, as well as the respiratory, endocrine, gastrointestinal, ocular, reproductive, immunological, and cardiovascular systems, all respond to noise in different ways [5]. Depending upon the many relationships between cortisol structures, the central and autonomic nervous systems (particularly the parasympathetic and sympathetic) react to noise in different ways [6]. Increased or decreased gastric motility, changes in gastric secretion, dyspepsia, and peptic and duodenal ulcers are the main effects of noise on the gastrointestinal system [7-8]. Numerous mediators are released during stressful noise situations, some of which have been shown to block stomach acid output via centrally mediated pathways.

The effects of stress on the digestive system are discussed in this article. Stress involved in pathogenesis of the most prevalent gastrointestinal tract illnesses is given significant attention. While there has been significant progress in identifying the genes linked to IBD (inflammatory bowel disease) predisposition, less is known about the environmental factors that cause the first presentation and subsequent relapses to noise stress, as well as the mechanisms by which they operate. Psychological stress is one environmental factor that has long been anecdotally reported to be associated with IBD activity [9]; recent research has made significant strides in establishing this association as well as in illuminating the mechanisms by which it takes place.

First, a definition of stress and an overview of the anatomy and physiology of the noise

stress response are given in this review. Before examining the evidence, the modern understanding of psychoneuroimmunology is reviewed. Both chronic stress, in the form of unfavorable life events, and acute experimental stress have been shown to affect the systemic immune and inflammatory function and increase disease activity in people with IBD. A living organism must continuously adjust to environmental changes at the molecular, cellular, physiological, and behavioral levels in order to preserve homeostasis. Any threat to the equilibrium of an organism is what is referred to as stress. The purpose of the stress response, which can involve both physiological and behavioral adaptations, is to maintain homeostasis [10].

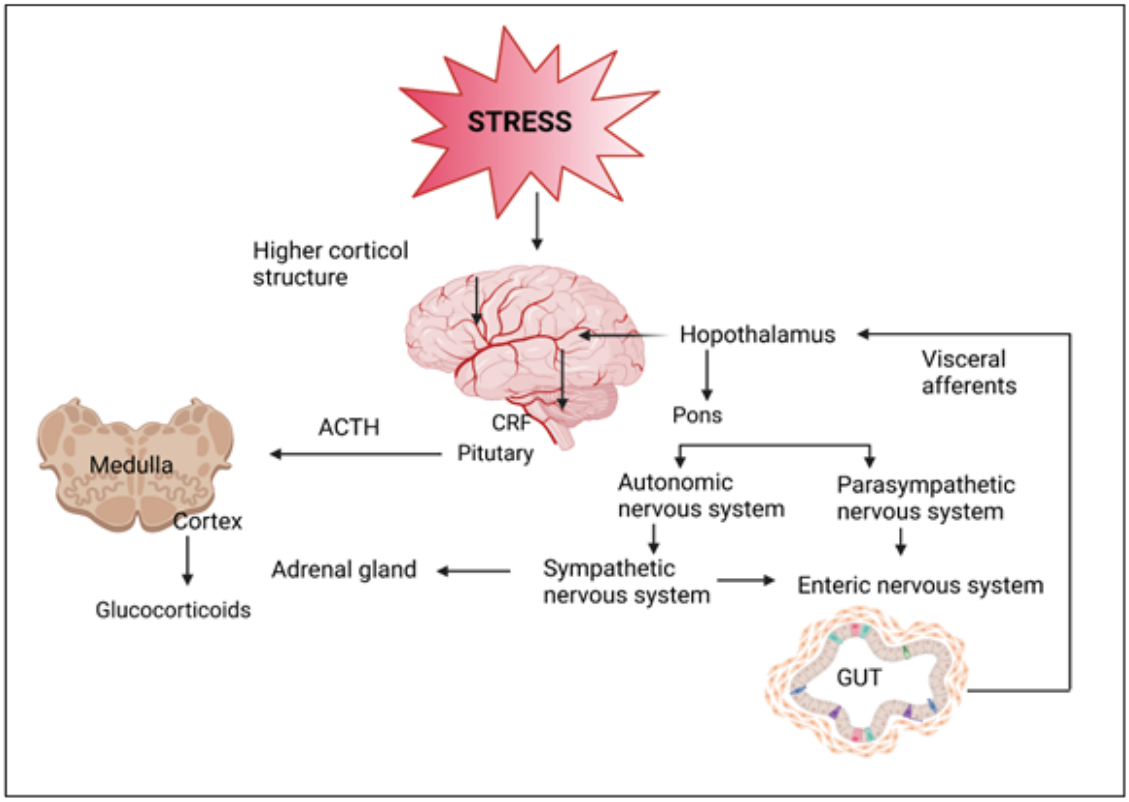

Figure 2: Pathways mediating the effects of stress on the gastrointestinal tract.

The hypothalamus, amygdala, and hippocampus are three particularly intertwined brain areas that are involved in the complex integration of the stress response. Higher cortical structures as well as visceral and somatic afferents provide input to this network. The HPA axis and the autonomic nerve system (ANS) are two interrelated effector pathways through which control the neuroendocrine stress response (**Figure 2**) [11]. Adrenocorticotropic hormone (ACTH) is released from the anterior pituitary gland when stress induces CRF production from the hypothalamus. Cortisol, the main glucocorticoid, is then secreted from the adrenal cortex as a result of this. The hypothalamus' direct descending neuronal routes to the pontomedullary nuclei, which regulate the autonomic response, are activated by stress. The adrenal medulla releases adrenaline and noradrenaline in reaction to stress by stimulating the sympathetic nervous system. While the vagus and sacral nerves offer parasympathetic input to the upper gut and, respectively, the distal colon and rectum, the sympathetic ANS neurons also directly supply the entire gut [12].

Online search strategies were employed here that included the use of several keywords, namely gastric secretion, stress, and behavioral changes. The principal search was accomplished by employing online search engines and databases, namely, PubMed, Google, Google Scholar, and ScienceDirect. In order to filter information, we used multiple or a combination of keywords to find expected reported

results. These were (a) noise + stress, (b) noise + stress + corticosteroid, and (c) noise stress + gastric secretion. The Web of Science was accessed for the reference-based literature articles.

2. Glucocorticoids (GCs) in the Biological System

The hypothalamic-pituitary-adrenal axis (HPA) regulates the plasma concentration of glucocorticoids (a type of steroidal hormone) and the adrenal cortex is responsible to release hormones for various physiological functionalities [13]. In addition to modulating the significant effects of biological processes, such as growth, metabolism, development, and immunological functions, GCs also assist in maintaining the body's physiology following stress [14–19]. Corticosteroid hormone synthesis is regulated by the HPA axis, which is provoked by both mental and physical simulations. The primary endocrinological properties of glucocorticoids maintain major effects on the following metabolic processes such as physiological metabolism (for lipids, proteins and carbohydrates), bone and cartilage formation, gastric secretion, cardiac functions, muscular functions, hydro-electrolyte balance, reproductive physiology, and hemo-lymphopoietic tissue formation [20]. Endogenous glucocorticoids regulate sleep and waking cycles, maintain nutrition through the stimulation of the hunger center, and have a significant impact on memory and learning functions by interacting with the receptors present in the hippocampus, prefrontal cortex, and basolateral amygdala [21]. Steroidal receptors are found throughout the brain's cognitive regions and are essential for the signaling process that involves dopamine and serotonin as well as other neurotransmissions. The hippocampus, which predominantly influences the limbic system and provides the platform for the flow of emotional information and memory, is where glucocorticoids may exert their possible effects in the CNS portion. Numerous investigations into the relationship between hippocampal atrophy and high levels of endogenous cortisol demonstrate that over-secretion of hormones has a negative impact on cognitive performance. The overproduction of cortisol caused by the corticosteroid's negative feedback loop assures that the hypothalamus pituitary-adrenal axis is activated, further damaging the brain's structures and the body's capacity to coordinate a proper response [22].

3. Effect of Noise on Cortical Levels

All noises are caused by noise in the environment. Numerous studies have demonstrated that environmental noise (including that from traffic, airplanes, and construction) has a negative impact on a number of physiological and psychological outcomes, including irritability, disturbed sleep, cardiovascular disease, hypertension, and stress [23]. The reaction being mediated so that stress is in the hypothalamic-pituitary-adrenal axis is the mechanism that is most frequently described (the HPA axis). This received a signal from a stress reaction and aids in the hypothalamus and pituitary gland's release of corticotropin releasing factor. Later, the adrenocorticotropic hormone encourages the adrenal cortex's release of cortisol through blood capillaries, which sets off reactions to a variety of stimuli. The release of neurohormones and neurotransmitters that affect the endocrine system as a result of cortisol secretion in response to stress limits the HPA axis' ability to function, which can lead to the onset of a number of stress-related disorders [24]. The ability and thresholds of the individual determine their level of noise sensitivity. The results and reactions to similar environmental noise exposure demonstrate a wide individual variance.

To be more specific, according to a study on how noise affects the body, the levels of IL-12 and INF (interferon) are linearly connected. It also implies that a rise in cortisol lowers the level of IL-12, which in turn lowers NK (natural killer cells) cells and the INF-α major marker of NK T-cell activation. So, it was concluded that an improvement in the cortisol levels eventually reduces immune function through the reduction of the activity of NK cells and NK T-cells [25]. Under normal (none stressed) conditions, the secretion of cortisol helps to fix myocardial cell activation and deactivation. It is easily characterized by the ECG in the morning, where high levels of cortisol exist later in the day when it gets reduced, but it reaches its lowest level at night. The circadian rhythm maintained by cortisol

can be disturbed by sleep patterns and psychological stressors like noise, stress of work and other environmental factors.

Research amplifies the role of cortisol in the many metabolic and homeostatic processes, moreover, it compensation with the stress, not only to the heart, blood pressure, blood lipids, glucose, blood clotting and blood viscosity, but also it is involved in many stress induced homeostasis events. However, the effects of long-term noise exposure, including occupational, road, railway, and air traffic noise on cortisol secretion are yet unknown. The variation in the amount of cortisol during the day could be an indicator of a disordered HPA axis control.

One of the pioneer groups in noise stress reported the role of salivary cortisol levels, which increase after high-intensity noise exposure. It was tested on fifty male volunteers, and the comparison was made with a statistically significant control group. The mechanism was proposed as an alteration in the HPA axis [26]. In another approach, Cantuaria and colleagues found a positive correlation between high road traffic noise and cortisol and cortisone (an inactive form of cortisol) levels in newborn children. A positive association was also observed in higher road traffic noise levels and the cortisol metabolite (i.e., β-cortolone) in between a positive response, a negative association was also prominent for other metabolites (i.e., α-cortolone and tetrahydrocortisol). These results were sufficient to draw attention to a potential link between early post-natal life changes in glucocorticoid metabolism and exposure to greater road traffic noise levels [27].

4. Effect of Noise on Gastric Secretions

The reputed 'Chae Yun Kim' group reported that short term aircraft noise caused a reduction in gastric acid secretion for about 60% of participants, an increase in gastric acid secretion in about 30% of participants, and the rest was found unaffected. It has been proposed that exposure to high-intensity noise can be responsible for gastric disorders in an individual [28]. According to the "Caboclo group," exposure to noise for 10 to 16 days significantly increased stomach acid output without changing gastrin levels. The findings demonstrated the critical role that cortical structures play in inter-digestive stomach acid secretion regulation in rats [29]. Holtmann et al. demonstrated a wide individual variation in gastric acid reaction to acute mental stress, and they discovered that this variation was partially linked to personality characteristics [30]. Tomei et al. revealed some of the surprising data regarding the secretion that sometimes remains unchanged, sometimes increased, or sometimes even decreased in relation to baseline gastric acid secretion that noise exerts by increasing gastric secretion. In the case of the subject whose baseline secretion was either low or high, noise produced an inhibitory effect.

It was also observed or postulated that the effect of noise on gastric secretion results from some action on the central nervous system (such as cerebral cortex, limbic system), the peripheral nervous system, and the neuroendocrine system, especially the neurohormonal part of the GI system. Research based on noise and gastric action concluded the role of noise is through the CNS via the corticosteroids and other responsible hormones. Stress has short and long-term effects on the functionality of the GI tract. Exposure to stress (due to noise) causes changes in brain-gut connections that result in several gastrointestinal associated problems such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and other functional gastrointestinal diseases. The gastrointestinal tract and the immune system are mostly receptive in the case of various stressors. It is a well-known fact that the impact of environmental and psychological stress-factors has become responsible for the pathogenesis of numerous gastrointestinal disorders [31]. Noise causing stress may influence various physiological actions of the GI tract, such as gastric secretion, mucosal permeability, visceral sensitivity, and mucosal blood stream [32, 33]. **Figure 3** depicts the mechanism of gastric acid secretion influenced by stress.

5. Exposure to Noise in a Rat Model

In a rat model, a study showed how road noise can have impact on gastric acid secretion [34] wherein 48

healthy rats were divided into five exposure groups to study traffic noise exposures: 1, 7, 14, 21, and 28 days and along with a control group. Using pentagastrin intraperitoneally, stomach acid was stimulated. The discharged gastric contents were then collected using a wash-out process, titrated, and released. Traffic noise exposure increased baseline and pentagastrin-stimulated stomach acid production compared to the control group after 1, 7, 14, and 21 days. However, following 28 days, induced adaptation caused both baseline and stimulated stomach acid output to decrease. Both in animals and people, exposure to noise has been demonstrated to cause disturbances in glucose homeostasis. Cui and coworkers demonstrated that continuous noise exposure increased blood glucose and hindered hepatic insulin production in an animal investigation intended to assess the effects of noise on the glucose metabolic process [35]. Rodents have provided excellent insight into the release of glucocorticoids in response to stress [36]. One of the major physiological functions of corticosterone, a primary glucocorticoid, enhances gluconeogenesis and hepatic glycogenolysis in rats, which leads to a higher availability of metabolic substrates to handle stressful situations [37].

6. Stress and the Brain-gut-microbiota Axis

The majority of people are aware of the close relationship between the stomach and the central nervous system, which is relevant to the association between stress and gastrointestinal disorders. It is commonly recognized that stress can cause a variety of gastrointestinal symptoms to develop, including dyspepsia, diarrhea, and abdominal pain. Beaumont's initial study on a wounded soldier with a stomach fistula revealed that anxiety or fury can have a major impact on gastric physiology, particularly acid output [38]. The regulation of physiological gut activities, such as the secretion, motility, and release of numerous neuropeptides and hormones, is greatly influenced by the ENS (enteric nervous system), often known as the "small brain" [39]. Corticotropin-releasing factor is a crucial coordinator of the endocrine, behavioral, and immunological reactions to stress (CRF). The CRF family of peptides exhibits strong biological effects and are expressed in the CNS and the stomach. The initial step in the activation of HPA involved in the stress response is CRF release in the hypothalamus. This is a key endocrine system that reacts to stress. Adrenocorticotropic hormone (ACTH) is released by the pituitary gland in response to CRF, causing the adrenal glands to secrete more cortisol, the stress hormone [40]. Stress alters the microbiome's genetic makeup and raises levels of proinflammatory cytokines and neurotransmitters, which may directly or indirectly affect the microbiota. Last but not least, long-lasting and excessive activation of CNS stress response regions is linked to chronic stress exposure. The brain regions responsible for feeling abdominal pain may undergo possibly permanent modifications as a result of this exposure.

7. Clinical Effects of the Brain-Gut-Microbiota Axis Dysregulation in the Upper GI Tract

As a result, the dysregulation of BGA brought on by stress exposure may result in the onset of a wide range of gastrointestinal conditions, including food allergies, gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), IBD, and IBS [41], [42]. The most significant GI tract manifestation of stress exposure is gastroesophageal reflux disease (GERD). It has been demonstrated that stress worsens GERD symptoms by inhibiting the lower esophageal sphincter and increasing acid sensitivity, or the sense of acid reflux. On the other side, a decrease in stress may cause GERD symptoms to improve [43]. Li et al. [44] and Perlman et al. [45] have shown in their recent studies the considerable influence of acute stress, such as the terrorist attack on the World Trade Center, on GERD symptoms. This is relevant to the relationship between stress and GERD. It has been established that stress exposure may be a factor in the development of this condition and may weaken the gastric and duodenal defenses against an attack from acid and pepsin damage [46].

Stress was regarded as one of the main risk factors for peptic ulcers before *Helicobacter pylori* (Hp) was discovered [47]. Stress ulcerations are a specific type of ulceration brought on by prolonged exposure to stress, and they are frequently seen in patients in intensive care units [48]. Practically speaking, both noninvasive and invasive procedures are used in the diagnostic process for stress-related illnesses of the upper GI tract [49]. Probiotics may have a beneficial effect on stress-related disease in the upper GI tract, according to some recent studies; nevertheless, the effects need to be further examined. Inflammatory bowel disease is also known to be induced by and exacerbated by stress (IBD). There is proof that stress either causes colitis to flare up or develop de novo [50]. Stress has been shown in numerous investigations to exacerbate experimental colitis by escalating oxidative damage [51]. Additionally, there is evidence to suggest that anxiety and stress have significant influence on bacterial growth, increasing bacterial adhesion and subsequent translocation due to enhanced barrier permeability. This could be a significant component causing the immune system to become activated, exacerbating or causing severe colitis [52]. The noise induced stress has detrimental effects on the body, which is the biggest reason for environmental pollution. The effect of the noise was described in conjunction with the corticosteroids, which eventually enhance the acid secretion. Acid secretion leads to the removal/damage of the protective wall of the intestine. Eventually, the results lead to a peptic ulcer. The review was presented in a way where almost all the reports with noise and the acids with reference to the hormones were taken care of in a systematic way. In a nutshell, noise induced gastric secretion was through some of inherent hormones, which can damage the body with some serious impact, and can lead to death. The noise in the metropolis or everywhere can be life threatening for humankind, which is the message here given through scientific logic to the reader.

8. Environmental Noise and Gastric Myoelectrical Activity

It is known that excessive environmental noise results in several health issues and related complications. There is an established relationship between the noisy sound and intestinal issues (such as gastritis, abdominal pain, and peptic ulcer). Other health issues include mental problems and cardiovascular diseases. However, little information is available regarding interactions between noise and gastrointestinal neuronal functionality. Gastric motility is regulated by gastric myoelectrical activity (GMA), which is about 3 cycles per minute for a sinusoidal wave in humans (as a normal value) [53]. This is measured by the standard EKG electrodes placed on the abdominal skin and presented as an electrogastrogram (EGG) [49]. Clinically, it is used to investigate dyspepsia in patients whose routine tests failed to define their complaints. Castle et al. (2007) investigated the effects of age and acoustic stress on the gastric GMA and autonomic nervous system in human subjects (males of ages 22–71 with a mean age of 44 years). GMA was recorded using a Synectics micro ripper. The authors concluded that GMA varies with age and that loudness can change the normal value of GMA, particularly in young candidates. Notably, even short term exposure to noise may alter gastric motility and secretion [49].

Zhen-Bin studied the impact of explosive noise on gastrointestinal transit and the plasma level of polypeptide hormones in rat models [50]. The authors found a range of sound intensity affecting the plasma level of polypeptide hormones (such as the vasoactive intestinal peptide, plasma motilin, and substance P) and gastrointestinal transit. Noise with a db value >80 accelerates the gastrointestinal transit of solid food, whereas a dB value >120 accelerates the gastrointestinal transit of liquid food [50]. Figure 3 illustrates stress causing gastric secretion mechanism while **figure 4** illustrates various plasma polypeptide hormones (μg/L) released after exposure to various levels of noise stimulation (dB) [50].

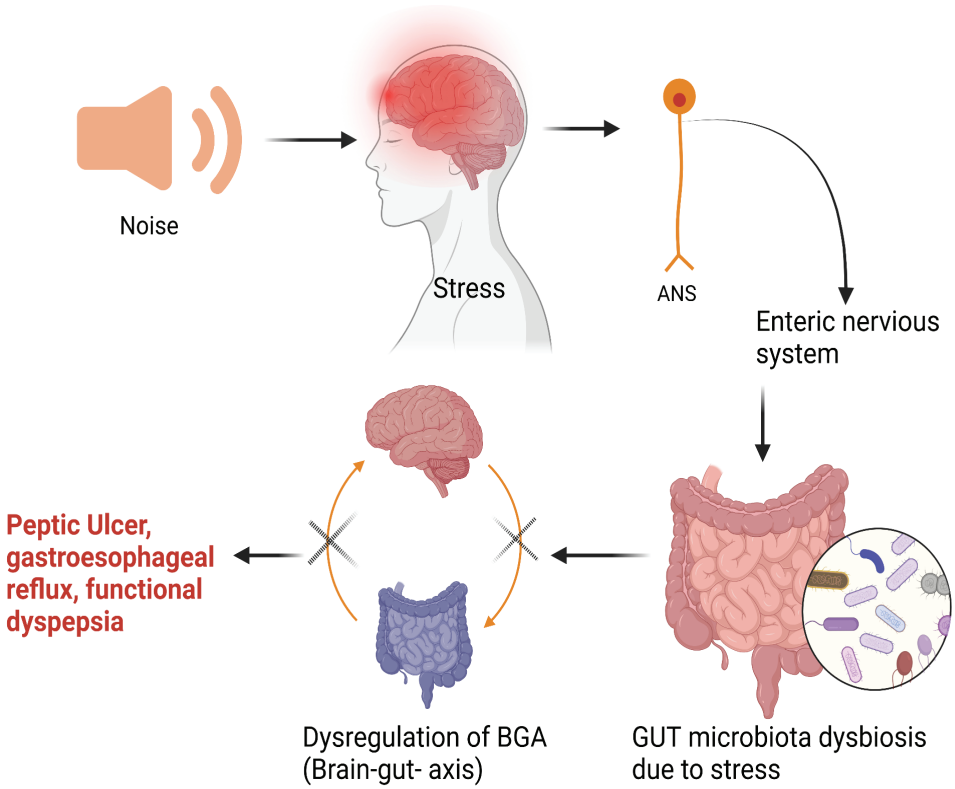

Figure 3. Stress causing gastric secretion mechanism

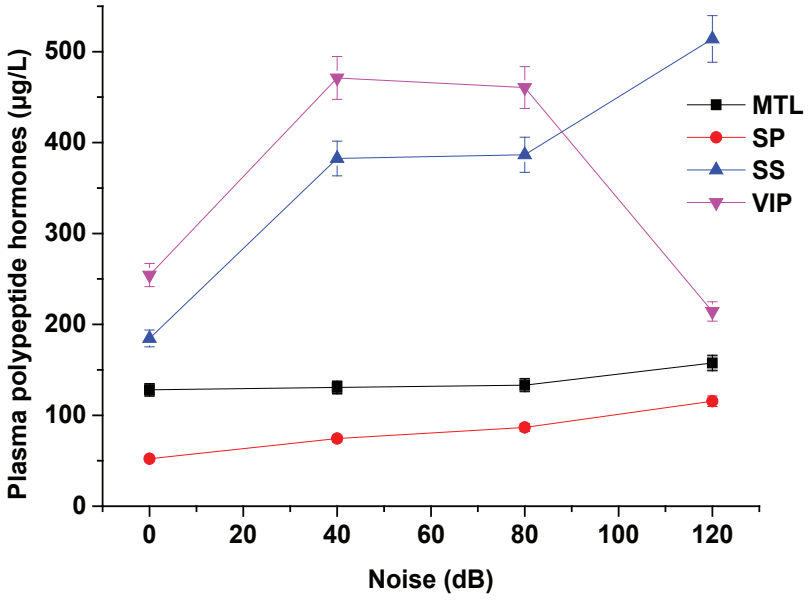

Figure 4. Various plasma polypeptide hormones released under various levels of noise stimulation in a rat model (n = 8, mean ± standard deviation)

Min and Min reported the connection between nighttime noise and peptic ulcers in humans, wherein 217,308 and 249,514 adults were included to study gastric ulcers and duodenal ulcers, respectively, during 8 years of regular follow-up [51]. They found that 32.1 % and 10.7% of subjects suffered gastric and duodenal ulcers, respectively, during follow-up. Thus, cumulative effect of environmental noise at night time affects the development of GI ulcer and damaging effects on GIT. Recently, Chi et al. (2021) reported that environmental noise stress disrupts the intestinal epithelial barrier to disturb commensal gut microbiota homeostasis by inducing oxi-inflammation and AD-like neuropathology in an EOAD (early-onset Alzheimer's disease) mouse model [52]. The authors concluded that long term environmental noise upregulates oxidative stress and systemic low-level inflammation, expanding our understanding of etiology of signaling pathways involved in brain and gut diseases. Thus, early detection of biomarkers can control detrimental effects on the brain after long term exposure to environmental noise [54, 55].

9. Treatment Strategies

The intestinal lining becomes damaged and inflamed and develops ulcers as a result of excessive stomach acid output. At the moment, serotonergic medications are among the most significant treatments. It has been suggested that certain pharmacological classes affect how serotonin behaves in the gut. The secretion, visceral sensitivity, and motility of enterochromaffin cells (ECC) are all significantly influenced by serotonin.

9.1 Antacids and Anticholinergic Drugs

After it was established that the stomach contains hydrochloric acid, antacid therapy gained popularity as a treatment for conditions like peptic ulcers that are caused by peptic acid. By neutralizing intraluminal acid, antacids including sodium bicarbonate, calcium carbonate, aluminum hydroxide, magnesium hydroxide, or combination formulations quickly offered efficient pain relief [56]. However, the duration of action of antacids in the human stomach is too brief to have a neutralizing effect. Antacid therapy is not typically used for current peptic ulcer treatment due to the availability of more effective and secure antisecretory medications, such as H_2-R antagonists and acid pump inhibitors. To prolong the effect of antacids, anticholinergic drugs, such as propantheline bromide and benactidine methobromide, have been concurrently administered to delay emptying of the agents into the duodenum. Anticholinergics can also inhibit acid secretion by themselves [57].

9.2 Histamine H2 Receptor Antagonists

Numerous organizations feverishly searched for an antagonist that could stop histamine from stimulating acid secretion because histamine was thought to be the final common mediator for acid secretion. The powerful H_2-R antagonists ranitidine, famotidine, and nizatidine were all created by altering the chemical structure of cimetidine, leading to a surprising cure for acid-related illness, including reflux esophagitis [58]. Later research revealed that both in humans and animals, these novel compounds inhibited gastric acid secretion induced by histamine as well as carbachol and gastrin. These results imply that the action of such secretagogues may require H_2-R stimulation. H_2-R antagonists have recently replaced other treatments for acid-related peptic disease, significantly enhancing the quality of life for many patients. Since the creation of H_2-R antagonists, pharmacotherapy for acid-related peptic diseases has significantly improved, but the drugs still have a number of drawbacks [59, 60].

9.3 Acid Pump Inhibitors

It was possible to create a new class of drugs that inhibit acid secretion thanks to the discovery that the acid pump H^+/K^+-ATPase is the last channel of gastric acid secretion. Surprisingly, research teams at the AB Hassle Company in Sweden found that isolated gastric glands from rabbit or guinea pigs could

be activated by dibutyryl-cAMP and that benzimidazole derivatives could effectively block stomach acid output. This result led to the theory that these substances might prevent parietal cell acid pumps from working [61, 62]. The cytoplasmic membranes of the parietal cell that is at rest contain the stomach acid pump, an ATPase. Upon activation, the pump moves to the canalicular membrane and pumps K^+ ions in exchange for H^+ ions into the canalicular space. Through food-stimulated and neuroendocrine pathways involving the activity of gastrin, histamine, pituitary adenylate cyclase-activating peptide, and acetylcholine, gastric acid secretion by the parietal cell is controlled. Therefore, altering stomach acid secretion could be done in a variety of ways. One potential strategy is to target the muscarinic receptors that acetylcholine uses to induce stomach acid secretion, however, muscarinic antagonists, like atropine, are not unique to the digestive system and have side effects like dry mouth and blurred eyesight. Histamine can bind to H_2 receptors and be blocked by competitive antagonists like cimetidine and ranitidine, but the parietal cell can still respond to other activating signals like acetylcholine. Despite the reasonable efficacy of histamine antagonists at night, all patients quickly develop tolerance, possibly as a result of the upregulation of other pathways [63, 64].

9.4 Several Inhibitors

Muscarinic antagonists, opioid inhibitors, CRF blockers, chloride-channel openers, and even melatonin are other medications that can be used to treat IBS [65]. This last class of medications exhibits beneficial antioxidant, anti-inflammatory, and anti-motility effects on IBS. According to relevant animal models, melatonin significantly reduces the worsening of colitis brought on by stress [66]. The primary symptoms should serve as the basis for pharmacotherapy. Antidiarrheal like loperamide are among the treatment choices for IBS (IBD-D), which has diarrhea as its main symptom. It is interesting to note that 5-HT_3 antagonists like alosetron, which is administered twice daily at a dose of 0.5–1 mg, have been demonstrated to be useful in treating diarrhea in IBS patients. Alosetron is, however, available in the USA to control severe IBS-D in females when used in conjunction with an approved risk management plan [66]. Rifaximin, a luminal acting antibiotic, recently showed a significant reduction in bloating in IBS-D patients, according to Pimentel et al. [67]. The use of laxatives (polyethylene glycol) and bulk agents (psyllium 2.5–30 g once a day) is another therapy option for IBS patients with constipation (IBS-C) [68-69]. IBS-C patients who received 1-2 mg of the selective 5-HT_4 agonist prucalopride once a day, saw relief from their constipation symptoms [70]. A prostaglandin E1 derivative called lubiprostone, with an approved dose of 8 mg twice daily for IBS patients, stimulates the mucosal epithelial chloride channels and encourages the production of chloride-rich fluid into the GI tract lumen. This causes the stools to soften and the colon transit time to quicken [71].

9.5 Antispasmodics

For IBS patients with bloating and pain, antispasmodics such as hyoscyamine sulfate (daily four times at the dose of 0.125 mg) and dicyclomine are recommended as the first line of treatment (10-10 mg twice daily up to four times daily). Antispasmodics primarily work as cholinergic receptor blockers, which reduce GI tract contraction.

9.6 Antidepressants

Moreover, various classes of antidepressants can mitigate the chronic pain of IBS patients through minimizing colonic contraction of smooth muscles. These drugs belong to fluoxetine (10-40 mg once a day), citalopram (20 mg daily), escitalopram (10 mg daily), sertraline (25-100 mg daily), and tricyclic antidepressants (TCA). By blocking their molecular absorption, TCA improves the bioavailability of serotonin and norepinephrine in the synaptic cleft. In contrast, SSRI (selective serotonin reuptake inhibitor) naturally inhibits serotonin reuptake [72]. Pregabalin and gabapentin have demonstrated effective benefits for controlling chronic pain perception in IBS patients [73]. Tricyclic antidepressants

(TCAs) are becoming more and more popular as peptic ulcer disease therapy options. TCAs have been demonstrated to be efficient and secure ulcer-healing medications in both placebo-controlled clinical trials and research that compares them to cimetidine. TCAs healing-producing mode of action is not well understood. TCAs have typically been found to reduce stomach acid output in human *in vivo* experiments. *In vitro* studies have shown that these drugs have strong H_1 and H_2 receptor blocking activities in addition to their well-known anticholinergic properties. The analgesic/depression effect of TCAs may be helpful in some patients with ulcers apart from these effects on acid output [74].

9.7 Probiotics

Probiotics may be utilized to cure stomach ulcers, according to numerous studies. The 1998 study by Elliott et al. gave rise to the concept of employing probiotics [75]. Gram-negative bacterial colonization occurred quickly at the site of the ulcer in a rat model of acetic acid-induced stomach ulcer, which greatly slowed ulcer healing. However, gram-positive bacterial colonization aided in ulcer healing. Notably, administering the exogenous probiotic strain *Lactobacillus* sped up the healing of ulcers. *Lactobacilli* and *bifidobacteria* strains found in probiotics may help with acid reflux and related problems. High-quality probiotics can benefit the microbiome in many ways, including GERD relief, improved digestion, improved bowel movements, support for immune function, and weight loss. Additionally, some probiotics may be helpful in treating diarrhea in IBS patients, according to recent studies. Probiotic dosage must be determined by additional research. The injured stomach epithelial cell lining can be improved by the application of probiotics. Finally, pre- and probiotics may help IBS patients with bloating and visceral hypersensitivity. The therapeutic advantages, however, appear to be strain-dependent [72]. More studies have recently shown that probiotics have a positive impact on IBS symptoms.

Recently, probiotics and prebiotics (combined and called as symbiotics) based treatment strategies have been explored to control stress induced GI discomfort by perturbing mucosal morphology, such as by improving barrier function, cultivating a favorable habitat for the gut microbiota, and boosting immunomodulatory effects [76]. Probiotics can come in a variety of species, strains, preparations, and doses, which makes it challenging to assess their effectiveness. Large-scale placebo-controlled trials will be required in the future to address all of these problems [77]. Recent research on stress-induced gastric mucosal lesions showed that utilizing a combination of probiotics (*Lactobacillus*, *Lactococcus*, *Bifidobacterium*, *Propionibacterium*, and *Acetobacter*) accelerated ulcer healing by reestablishing the ratio of pro- to anti-oxidants in the stomach mucosa [78]. Additionally, probiotic combinations (comprising *Bifidobacterium animalis* VKL and VKB with or without *Lactobacillus casei* IMVB-7280) improved the recovery of stress hormones (adrenocorticotropin and corticosterone), decreased proinflammatory cytokines, and boosted anti-inflammatory cytokines [79].

A combined clinical and basic science experimental approach is likely to produce significant strategies to maximize the use of probiotics in health and disease, taking into account the probiotic strains, dosage, commercial preparations, and the heterogeneity of patients [80]. Some genetically modified probiotic strains with particular skills for the release of anti-inflammatory cytokines, vaccines, and anti-pathogenic compounds have been created using novel methods [81, 82]. In order to create live mucosal vaccines for a variety of antigens generated from bacteria, viruses, and parasites, engineered *Lactococcus lactis* strains were created [83]. Additionally, rotavirus spike protein subunit VP8 was produced using recombinant *Lactococcus lactis* strains to help prevent rotavirus infection [84]. Probiotics have the potential to be used in the future as delivery systems for gastrointestinal mucosal lesions. Pharmabiotics are a new targeted medicine delivery method that uses probiotics [85].

10. Conclusion

Noise induced stress has detrimental effects on the body, which is the biggest reason for environmental pollution. The effect of the noise was described in conjunction with corticosteroids, which eventually

enhance acid secretion. Acid secretion leads to damage of the protective wall of the intestine. Eventually, the results lead to a peptic ulcer. The review was presented in a way where almost all the reports with noise and resulting acids with reference to hormones were taken care of in a systematic way. In a nutshell, noise induced gastric secretion was through some inherent hormones, which can damage the body with some serious impact, and can lead to death. Noise in the metropolis or everywhere can be life threatening for the human race, which is the message given through some scientific logic to the reader. An excessive amount of gastric acid secretion leads to damage to the intestinal microflora. Therefore, the application of synbiotics (a mixture of probiotics and prebiotics) can provide a healthy microbiota. Conventional treatment options are showing several systemic side effects, so researchers have focused on the application of novel drug delivery systems along with synbiotics, although the application of synbiotics needs to be performed in a large population for more efficient outcomes.

Abbreviations

HPA: hypothalamic-pituitary-adrenal axis, CNS: central nervous system, gIL-12: Interleukin 12, NK cells: Natural killer cell, INF-α: Interferon alfa, IBDGI: Gastro intestinal, inflammatory bowel disease, IBS: irritable bowel syndrome, ACTH: Adrenocorticotropic hormone, PUD: peptic ulcer disease, GERD: gastroesophageal reflux disease, GMA: gastric myoelectrical activity, EGG: electrogastrogram.

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