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NARRATIVE REVIEW Open Access

Exploring The Tasting System and Clinical Significance of Taste Disorders: A Narrative Review

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Abstract

Introduction: This review took an in-depth look at the intricate anatomy of taste buds, unveiling their complex structure and function, delved into the fascinating mechanisms that underlie taste transmission, shedding light on how sensory information is relayed from the taste buds to the brain, enabling us to perceive and differentiate various flavors.

Result and Discussions: This narrative review indicates that diverse factors can induce changes in taste buds, ranging from genetic predispositions to external influences such as medications and lifestyle habits. By comprehensively understanding these factors, healthcare professionals and researchers can better identify the root causes of taste problems and devise effective management strategies. Recognizing the clinical significance of taste-related issues is crucial in providing appropriate care and support to individuals experiencing taste disorders.

Conclusions: Despite significant advancements in understanding the gustatory function and molecular mechanisms of taste receptor cells, there still needs to be a comprehensive clinical understanding regarding the underlying causes and mechanisms of taste disorders in humans.

Keywords: Tasting System - Taste Disorder – Gustatory - Clinical Significance

INTRODUCTION

The sense of taste is one of the fundamental human senses, providing valuable information about the flavors we encounter and helping us identify harmful substances.[1] Taste receptors on the taste buds are distributed throughout the oral cavity, pharynx, larynx, and esophageal inlet.[2,3] In the past, it was believed that different tastes were localized to specific areas on the tongue. Still, research has shown that sweet, sour, salty, bitter, and umami flavors can be detected all over the tongue.[4] The back of the tongue is particularly sensitive to bitter tastes, which protects us from ingesting potentially harmful substances.

Taste perception is a complex process involving taste receptors activating sensory cells, releasing chemical messengers to trigger neural pathways.[4,5] Contrary to common perception, taste is not solely a sensation experienced on the tongue but rather a combination of olfactory, gustatory, and trigeminal sensations. These signals are transmitted to the brain, where chemical components are integrated with various sensory systems, including those governing homeostasis, visceral responses, memory, emotions, and language processes.[4]

Although taste and aroma are often used interchangeably, they are distinct sensory experiences. While not life-threatening, taste disorders can cause discomfort, leading to issues such as loss of appetite and changes in eating behavior that may have health consequences. Various factors can affect taste bud function, including genetics, chemicals, medications, trauma, surgery, smoking, alcohol use, and radiation therapy.[7,8]

Individuals with taste disorders face challenges in enjoying food and beverages, impacting their overall quality of life beyond mere nutritional concerns. Unfortunately, diagnosing and treating taste disorders remains challenging, necessitating greater awareness among the general population and the medical community.[6,7] This review emphasizes the importance of accurate assessment and diagnosis for effective treatment. It explores unresolved aspects of taste disorders and intriguing findings related to their management, focusing on current pharmacological options. Raising awareness and understanding of taste disorders are vital to providing better support and solutions for those affected.

THE FUNCTION OF THE TONGUE

The tongue is a remarkable muscular structure found within the oral cavity. It is intricately connected to various bones and tissues, including the hyoid bone, mandible, mastoid process, palate, and pharynx, through a network of muscles. This complexity enables the tongue to perform a wide range of functions. The tongue can be divided into two distinct parts: the anterior and posterior sections. The posterior part forms an interesting V-shaped groove known as the terminal sulcus, which adds to the unique anatomy of this versatile organ.[9,10] The tongue serves multiple essential roles in both sensory perception and motor functions for speech and swallowing. It plays a crucial role in detecting various flavors as a taste organ. These flavors interact with taste receptors present on the tongue's taste buds, leading to the transmission of distinct taste sensations. Five primary taste receptor categories exist: sweet, salty, sour, bitter, and umami.[10] Producing sound involves skillful manipulation of the tongue against the teeth and the palate within the oral cavity. Crucial for sound production is the internal muscles of the tongue. The tongue skillfully moves food around the mouth to facilitate chewing, applying pressure against the hard palate.

Moreover, during the preparatory phase, the tongue assists in forming a cohesive food bolus and initiates the swallowing reflex.[2,11]

ANATOMY OF THE TASTE SYSTEM

Taste is perceived through chemosensory receptors called taste buds. The taste buds are onion-shaped structures containing 50-120 taste cells. They comprise a basement membrane and fuse at their apical projections, forming the sensory epithelial organ.[2,3] The microvilli on the apical protrusions are the actual taste receptors, which connect to ion channels in the apical and lateral membranes and are responsible for the perception of taste stimuli.[4,11] The nucleus is located in the lower third of the taste bud, where most afferent nerve terminal fibers are. Taste buds regenerate rapidly, with an average life span of 8-12 days.[12]

Taste buds are found in the oral cavity, pharynx, larynx, and upper esophagus. The most significant number of taste buds is located on the dorsal surface of the tongue, approximately 4,600, of which 48% are circumvallate papillae, 28% are foliate papillae, and 24% are fungiform papillae. At the same time, the remaining 2,500 are distributed elsewhere. Electron microscopic analysis shows that taste buds comprise type I, II, III, and IV cells with different ultrastructural characteristics. Several studies have addressed the functions of these types of taste buds.[2,12]

PHYSIOLOGY OF THE TASTE SYSTEM

The taste system is vital in detecting and conveying various tastes experienced in the mouth. Some tastes, such as sugars, amino acids, salt, and fat, hold nutritional value, which can stimulate appetite. Conversely, certain tastes like atropine, quinine, and nicotine are repulsive. However, the gustatory system is limited to perceiving only a few distinct taste qualities: sweet, umami, bitter, sour, and salty. Intriguingly, the rich and complex taste experiences result from integrating taste with other sensory elements like smell, texture, pungency, and temperature. Texture, pungency, and temperature, which add depth to our taste experiences, are processed by the somatosensory system, particularly the trigeminal system. Alongside the gustatory system, the trigeminal nerve innervates the perigonal epithelium, enabling the transmission of temperature, mechanical stimuli, and sensations of pain or cold. These intricate systems work harmoniously to create the diverse flavors and sensations we perceive while eating and drinking.[9]

Transduction of taste

When external stimuli enter the mouth, they interact with the microvilli in the taste pore. The taste receptor proteins are primarily situated on the apical surface of the taste cell.

At the same time, the transduction system, involving ion channels, is distributed across both the apical and basolateral membranes. Specific ion channels are located on the basolateral side of the taste cell to perceive salty and sour tastes. These channels consist of Na+, K+, and Ca2+ ions and play a crucial role in depolarization when the taste cell responds to chemical stimuli. Furthermore, for sweet and bitter tastes, the stimuli can also interact with protein components like cyclic AMP. Upon entry of the stimulus into the taste cell, an alteration in the cell's electrical state occurs, leading to the release of neurotransmitters and the subsequent activation of nerve fibers. This intricate process enables the transmission of taste signals to the brain, ultimately contributing to the perception of different taste qualities.[13,14]

Sweet, umami, and bitter tastes

Various chemical compounds, including natural sugars like glucose, fructose, sucrose, and maltose, and artificial sweeteners such as saccharin, aspartame, and cyclamate, can trigger the sweet taste receptors. Sweet amino acids like D-tryptophan, D-phenylalanine, D-serine, and sweet proteins like monellin, brazzein, and thaumatin also activate these receptors. Sweet taste transmission occurs through the activation of G protein-coupled receptors (GPCRs) located on the apical surface of the taste cell. The essential taste receptor families involved in this process are T1R2 and T1R3. Once these GPCR receptors are activated, calcium is released from intracellular stores, and a signaling cascade results in an increased uptake of sodium. This complex mechanism allows our taste buds to perceive and differentiate the delightful taste of sweetness in various substances.[15,16] In the case of artificial sweeteners such as saccharin, a different GPCR is activated, which activates phospholipase C (PLC) to form IP3. Increased IP3 levels increase intracellular calcium concentration.[17] The alterations in ions lead to cell depolarization, resulting in the opening of particular ATP channels. This allows ATP to enter the synapse and influence the afferent taste axons.[9,16] Umami taste receptors are composed of T1R3 protein, similar to sweetener receptors, but they pair with T1R1 protein. Once the G-protein receptors are activated, they initiate the transduction pathway. Bitter taste receptors are classified under the T2R receptor protein family. Interestingly, each taste cell can express most, if not all, different types of receptors, enabling it to detect various molecules crucial for identifying and avoiding harmful substances.[18] The activation of G-protein receptors triggers a signaling cascade, leading to an increase in intracellular calcium levels. This, in turn, opens ion channels, causing a flow of sodium into the cell, which results in cell depolarization. Consequently, specific ATP channels are opened, allowing ATP to enter the synapse and influence the afferent taste axons. This intricate process ensures that our taste system can accurately interpret and respond to various tastes, including bitter flavors that may signal potentially harmful substances.[19]

Salty and sour tastes

Epithelial sodium channels mediate the perception of salty tastes. These receptors are typically open, and when we consume foods with high salt concentrations, sodium flows into the cells, resulting in depolarization. Consequently, voltage-gated sodium and calcium channels are available due to this change. The increased influx of calcium then triggers the release of vesicles containing serotonin. Subsequently, serotonin acts on afferent axons, leading to depolarization and initiating action potentials. This intricate process ensures that our taste system accurately detects and responds to salty flavors.[20]

The recognition of sour taste depends on cells that express Polycystin 2 Like 1, Transient Receptor Potential Cation Channel (PKD2L1), which is associated with the III-type cells. Sour taste sensations are triggered by acidity, wherein acidic substances in water release hydrogen ions (protons). These protons enter ion channels, leading to the blocking of potassium channels. As a result, there is a reduction in potassium efflux, and the presence of protons depolarizes the cell, causing voltage-gated sodium and calcium channels to open. The increased intracellular calcium levels subsequently trigger the release of serotonin in the synapse. This complex process ensures our ability to effectively perceive and respond to sour tastes.[21]

Central taste pathways

Three cranial nerves play a role in innervating the tongue: the cranial nerve VII covers two-thirds of the tongue. In contrast, the cranial nerve IX is responsible for the posterior third. Additionally, the superior laryngeal branch of cranial nerve X innervates the epiglottis and pharynx. These cranial nerves enter the brainstem through the spinal cord and synapse in the nucleus of the tractus solitarius. The information is then transmitted to the ventral posterior medial nucleus in the thalamus, which further relays it to the gustatory cortex located in the insula region of the lateral sulcus. For conscious taste perception, information is also conveyed to the somatosensory cortex. Meanwhile, the hypothalamus, amygdala, and anterior insula frontal operculum are involved in the affective component of taste. In the central pathways, taste nerves typically inhibit each other to maintain balance. However, if one nerve is damaged, inhibitory impulses on that side decrease, leading to an increased response on the opposite side. Fortunately, damage to these nerves rarely results in completely losing taste perception. Unlike the taste system, the olfactory system depends on a single nerve, making it more vulnerable to damage and disruption of smell perception.[3,14]

MEASUREMENT OF THE TASTE DISTURBANCE

Quantitative assessment of taste disorders involves several tests that can be categorized into chemical and electrical stimuli. Chemical tests utilize natural stimuli and chemical taste substances to evaluate taste perception, while electrical tests involve applying an electrical stimulus to the tongue's surface. Standard chemical tests include the three-drop method, taste tablets, filter paper disks, and taste strips. Electrical tests include electrogustometry and gustatory evoked potentials. Additionally, imaging techniques such as functional MRI (fMRI), positron emission tomography (PET), microscopy, and photography can be employed. Taste testing is valuable for both research and diagnostic purposes.[22]

Diagnosing a taste disorder is critical to deciding on appropriate treatment. Thoroughly evaluating the patient's medical history is essential to identify possible factors contributing to the taste disorder. In addition to performing formal tests to evaluate olfactory and gustatory sensation and, if possible, the trigeminal nerves, a comprehensive clinical examination of the ear, nose, throat, and neurologic systems is required. In cases where central nervous system involvement or idiopathic taste disorders are suspected, imaging studies may be warranted. When examination and imaging findings are normal, it is essential to pay attention to routine analysis of blood samples to detect significant metabolic disorders or deficiencies (e.g., iron, thyroid, renal, or hepatic dysfunction and vitamins) and underlying immunologic disorders (e.g., Sjoegren's syndrome, sarcoidosis, inflammation).[14,22]

CONDITION AFFECTING THE TASTE SYSTEM

Age

Increasing age affects the decline of the sense of taste. After the age of 60, the sense of taste gradually decreases. The decreased sense of taste in the elderly is caused by a decrease in taste receptors related to the physiology of aging and the effects of drug use. Medications commonly taken by the elderly include cardiovascular drugs, corticosteroids, psychotropic drugs, and metabolic drugs, all of which cause taste changes.[8] The underlying mechanism is still controversial, but it is known that the drug affects both the peripheral and central nervous systems and alters salivary flow and the buffering system. Poor oral hygiene, such as oral cavity infections, can damage the central and peripheral nerves.[23] Conditions such as inadequate dietary intake and deficiencies of thiamine, vitamin C, and dietary fiber may increase taste sensitivity in the elderly.[6,24]

Previous studies have found that umami, sour, and bitter tastes are most commonly affected. Jeon et al. and Alia et al. found that sweetness was least affected by age. Saliva plays an essential role in salty and sour tastes by adding molecular ionization and affecting taste levels.[23,25]

Systemic diseases

Systemic diseases such as diabetes, hypothyroidism, liver disease, kidney failure, etc., can affect taste. People with diabetes experience neuropathy, which affects the taste buds and leads to changes in the taste buds. Systemic medications such as antihypertensive drugs and chemotherapy also affect the taste buds.[7,8] Chemotherapeutic agents are known to lower the threshold for bitter taste. Radiation also affects taste buds by damaging the mechanism of taste pores. It takes about six months to restore the function of taste buds.[26]

Damage to the nerves

Nerve damage results from surgical procedures that put pressure on the taste buds, such as tonsillectomy, middle ear surgery, or resection of a nerve associated with a tumor. Taste disturbances after tonsillectomy have been reported in 10-20% of patients. In tonsillectomy, indirect damage to the lingual branch of the glossopharyngeal nerve can lead to taste disorders. In most patients, the glossopharyngeal nerve runs laterally from the superior pharyngeal constrictor muscle and is thus separated from the palatine tonsils.[27] The nerve damage is temporary or transient because the taste buds overlap, so that taste is hardly disturbed in everyday life.

CLINICAL SIGNIFICANCE

Disturbances in the sense of taste can lead to poor mental health and affect the quality of life. Taste allows us to identify critical and potentially harmful substances for nutrition; thus, it is essential to identify and treat taste disorders. However, taste disorders are often accompanied by other symptoms, leading to neglect of the disorder itself. Shaikh et al. found that when asked, "Do you have problems with taste?" only 10% of patients with taste disorders were identified. Therefore, it is important to investigate this issue further and ask patients specific closed-ended questions to obtain an accurate history.[22]

Patients commonly experience taste disorders categorized as either qualitative or quantitative. Individuals often notice qualitative disorders as they cause permanent or intermittent distortions in taste sensations, impacting daily life. On the other hand, quantitative disorders may not elicit strong complaints. Interestingly, many individuals may have decreased taste function without awareness, emphasizing the importance of assessing gustatory function. Many patients may present with mixed complaints, encompassing qualitative and quantitative aspects. The term "dysgeusia" is commonly used to describe taste disorders, primarily distorted taste perception.[7,28]

In the realm of taste disorders, various classifications exist, primarily based on clinical presentation, either considering the site of the lesion or the most likely cause. When lesions occur beyond the NTS (nucleus tractus solitarius), they are called peripheral taste disorders. At the same time, those impacting the NTS and proximal regions fall under central nervous system lesions. In current clinical practice, taste disorders are often categorized according to their probable causes, making it easier to diagnose and manage them effectively. These probable causes fall into several major etiological groups, including neural injuries, deficiency states, medication side effects, post-infectious conditions, systemic diseases, and idiopathic cases where the cause remains unknown. A thorough patient history becomes paramount in exploring and identifying these potential factors contributing to taste disorders. Treating taste disorders significantly depends on pinpointing the underlying cause, underscoring the crucial role of accurate diagnosis in providing appropriate and targeted interventions.[6]

Neural injuries can cause both qualitative and quantitative taste disorders and can stem from various factors such as trauma, inflammation, radiation, stroke, or surgical injuries. Metabolic and systemic diseases significantly impact the gustatory system, often leading to taste disorders. Medications also play a significant role in inducing qualitative taste disorders. For instance, angiotensin-converting enzyme inhibitors, commonly prescribed for hypertension and cardiac failure, can cause such disorders by elevating local bradykinin levels and leading to zinc and copper deficiencies. Diuretics like amiloride, spironolactone, and furosemide, as well as lipid-lowering agents such as atorvastatin and simvastatin, are also known to impact taste perception. In some cases, rare causes of dysgeusia can be attributed to specific food components like pine nuts or paraneoplastic symptoms. Sweet dysgeusia, in particular, requires careful investigation as it has been associated with being an early symptom of lung or thymus cancer. Despite thorough evaluation, there are instances where patients are eventually diagnosed with idiopathic taste disorders, indicating that no specific cause could be identified even after ruling out other possibilities. This highlights the limited clinical understanding and the challenges that the field of taste disorders needs to address in the future. Continued research and advancements are essential to improve our comprehension and management of taste-related issues.[9,14,22]

Burning mouth syndrome (BMS) is a specific type of taste disorder characterized by a burning sensation, dryness, and often painful discomfort in the mouth. Of note, only about 30% of BMS cases are accompanied by taste complaints.[29,30] This condition is more commonly seen in post-menopausal women, although the exact cause is still unclear, with psychological factors thought to exacerbate symptoms. Recent studies in neurophysiology, psychophysics, pathology, and functional MRI have proposed various neuropathological mechanisms as potential explanations for primary BMS. From experimental evidence, several hypotheses have emerged, proposing that BMS could be linked to peripheral neuropathy, central neuropathy, or even manifest as a phantom pain symptom.[31] Loss of tiny nerve fibers in the oral cavity has been identified as a critical factor in the pathogenesis of BMS. However, the specific cause of this nerve fiber loss remains unknown. It is important to note that BMS affects taste perception through the interaction between the affected sensory and nearby trigeminal taste fibers, suggesting that it is not exclusively a taste-related pathology.[32] Therefore, treating BMS is more similar to treating chronic pain disorders.

TREATMENT OPTIONS

It is important to note that the treatment of taste disorders depends on their underlying cause, and there needs to be more extensive research on effective treatments.

Non-Pharmacological Approaches

Spontaneous Recovery. Unlike other sensory systems, the sense of taste has a high rate of spontaneous recovery, thanks to the natural regeneration process in both healthy and diseased states. While the recovery rates are generally high, it can take up to two years to fully recover. Patients should be informed about this timeline; regular follow-up is necessary to monitor progress. In cases of nerve injury or post-infectious taste impairment (including COVID-19-related cases), the initial approach is to inform the patient and wait for spontaneous recovery. If spontaneous recovery does not happen, pharmacological treatments can be considered.[27,28]

Discontinuation of Medication. When taste disorders are caused by medication or food side effects, the most effective treatment is discontinuing the offending medication. However, it may take several days or even months for taste function to return to normal after discontinuation. For example, terbinafine, an oral antifungal drug, is known to cause taste disorders approximately 3-5 weeks after starting the medication. Once the medication is stopped, taste function can take 5-6 weeks to normalize.[6,33]

Transcranial Magnetic Stimulation. Repetitive transcranial magnetic stimulation (rTMS), a widely utilized therapy for depression, has shown promising results in addressing smell and taste disorders. Despite its effectiveness, rTMS has not yet been established as a standard treatment for taste disorders in the realm of clinical practice.[34]

Pharmacological Treatments and Quality of Trials

Compared to other areas of medicine, there is limited knowledge and few studies on pharmacological treatment options for taste disorders. Currently, clinicians dealing with taste disorders primarily focus on diagnosing and identifying the underlying causes. Consequently, only a few authors have conducted prospective studies on pharmacological treatments for idiopathic gustatory dysfunction. Some anecdotal reports and small-scale studies have suggested successful treatments using ice cube suction, local anesthesia, theophylline, alpha-lipoic acid, or vitamin D supplementation. However, there is a need for more comprehensive research and larger-scale trials to establish evidence-based pharmacological treatments for taste disorders.

Several studies have indicated a connection between mood states and taste complaints. Positive mood states have been associated with better spontaneous recovery rates in patients with idiopathic dysgeusia than those with depressive symptoms. Cognitive-behavioral therapy has also shown positive effects on glossodynia and dysgeusia, and there is evidence of a correlation between depression and taste function. Treatment of depression appears to impact taste disorders, suggesting that dysgeusia may be a symptom of mild depression. Interestingly, antidepressants have been found to affect taste function not only in disease but also in healthy individuals.[34,35] Selective serotonin reuptake inhibitors and noradrenaline have improved human taste thresholds. It remains unclear whether taste disorders can cause depression or if taste disorders sometimes accompany depression. While neuro-modulators such as clonazepam have shown efficacy in certain oral disorders like burning mouth syndrome (BMS), there are only anecdotal reports suggesting the successful use of drugs like amitriptyline[36], valproate[37], and gabapentin for pure taste disorders unrelated to BMS.[38] These cases highlight the need for more substantial evidence and research in the pharmacological treatment of taste disorders.

Zinc is the most extensively researched treatment option suggested for addressing idiopathic taste disorders. Although zinc has demonstrated success in treating postoperative taste disorders based on case reports, multiple double-blind, randomized clinical trials support its effectiveness for idiopathic taste disorders. These studies consistently show significant improvements in taste disorders through the supplementation of zinc gluconate. The initial trial conducted by Yoshida et al., followed by subsequent studies led by Heckmann et al., exhibited clear enhancements in taste disorders after three months of daily oral intake of zinc gluconate (140 mg).[39] Zinc gluconate therapy has shown promise as a treatment option for idiopathic taste disorders, with relatively mild side effects like nausea and gastrointestinal problems observed only at higher doses than those used in reported regimens. This indicates that zinc gluconate can be considered a safe and viable option for treating taste disorders.[40]

In addition to zinc gluconate, the effectiveness of zinc has also been supported with a zinc-containing molecule called polarizing. However, there seems to be a lack of direct correlation between serum and saliva zinc levels, symptoms, and treatment response in patients with taste disorders. Some patients may experience taste disorders despite having normal serum zinc levels, while others with zinc deficiency may not report any taste-related complaints. This complexity makes it challenging to pinpoint the exact mechanisms by which zinc exerts its therapeutic effects. Various hypotheses have been proposed to explain the efficacy of zinc in treating taste disorders. One theory suggests that zinc might serve as a crucial co-factor for saliva proteins, influencing the growth and turnover of taste cells. Another hypothesis ties zinc's antidepressant properties to its observed effects. It has been noted that zinc can enhance the effects of antidepressant drugs, and there is speculation that zinc alone might have mild antidepressant properties. Clinical trial data by Heckmann et al. supports this notion, as the zinc-treated group showed significant improvement in Beck Depression Inventory scores compared to the placebo group. This suggests that zinc's antidepressant properties may positively influence taste function in healthy individuals and those with taste disorders. However, it's worth noting that the same doses of zinc proven effective in treating taste disorders did not exhibit preventive or protective effects in a double-blind trial on chemotherapy-induced taste disorders. This indicates that zinc treatment may be most suitable for idiopathic taste disorders rather than those caused by chemotherapy. Another interesting finding regarding zinc's role in taste pathophysiology is the correlation between reported drug side effects and their zinc-chelating properties. Drugs with a higher affinity for chelating zinc are more likely to cause taste side effects. This suggests a potential connection between zinc availability and taste disturbances caused by certain medications.[6,41]

CONCLUSION

While taste and aroma are frequently used interchangeably, it is important to recognize that taste encompasses more than just the sensation the tongue perceives. It is a multifaceted amalgamation of olfactory, gustatory, and trigeminal sensations. These sensations are intricately transmitted to the brain, where chemical components interact and integrate into the sensory system, intertwining with homeostatic, visceral, memory, emotional, and language processes. Although not life-threatening, taste disorders can significantly impact an individual's quality of life. Unfortunately, they often go undiagnosed, leading to discomfort, such as loss of appetite and alterations in eating behavior, which can have adverse health consequences. Various factors contribute to the malfunctioning of taste buds, including genetic and chemical factors, medications, trauma, surgery, smoking habits, alcohol use, and even radiation therapy. Unfortunately, our understanding of distinguishing between different types of taste disorders is limited. Extensive research endeavors are needed to enhance the accuracy of diagnostic procedures and increase the effectiveness of therapeutic interventions for individuals with taste disorders.

CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest concerning the publication of this article.

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