Scientific Research Publishing

World Journal of Neuroscience, 2021, 11, 246-266
https://www.scirp.org/journal/wjns
ISSN Online: 2162-2019
ISSN Print: 2162-2000

A Neurobiological Examination of Environmental, Subjective, Peripheral and Central Taste Sensation Processing Variances Associated with Taste Alterations: A Case Study Method

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How to cite this paper: Ben-Abraham, T.N. (2021) A Neurobiological Examination of Environmental, Subjective, Peripheral and Central Taste Sensation Processing Variances Associated with Taste Alterations: A Case Study Method. *World Journal of Neuroscience*, **11**, 246-266.
https://doi.org/10.4236/wjns.2021.113018

Received: June 21, 2021
Accepted: August 16, 2021
Published: August 19, 2021

Abstract

This study examines a common phenomenon that is greatly ignored by the clinical community for numerous reasons. Many people for a multitude of reasons experience taste alterations. The supertaster phenomenon is an alteration of taste that requires more investigation. In this study, a proband was examined for subjective reports of a taste alteration to determine its nature through a medical history examination and interview as well as any recollections of the taste disorder in her life. Through this examination, it was found that medical history examination and interview of the proband that many members of her nuclear family showed traits of the same taste disorder or in the case of one family member being a suspect for the taste alteration and one member not showing any signs because of genetic diversity as a half-sibling. Taste disorders are heritable, have multiple health and mental health consequences, influence life choices including mate choice, avoidance behaviors, social choices, alcohol use/abuse, smoking, food choices, and more. More awareness is needed in the research and clinical community into taste alterations as well as calls for future research from neuroscience, biomedical science, life science, and allied science community to investigate taste alterations.

Keywords

Gustatory Neurobiology, Taste Disorder, Supertaster Phenomenon, TAS2R38 Gene

1. Introduction

Taste is a special sense in mammals, especially humans, that guides food choices [1]. One example of taste guiding preferences is the fact that humans have adapted to prefer sweet tastes [1]. Evolutionarily, a bitter taste is a sign of a dangerous substance such as a poison; a sweet taste is a sign of a high energy food containing carbohydrates, and an umami taste is a sign of high protein food [2]. Tastes are sensed by a specific organ known as the tongue.

The tongue is the primary organ for sensing taste. The tongue contains a finite number of receptors that conduct specific taste sensations from the tongue to the brain and these specific receptors sense sweet, sour, bitter, umami, and salt tastes [1]. In terms of neurobiology, how is it transmitted to the brain? When these receptors pick up on a certain taste sensation from the tongue, the sensation is transported to the primary gustatory cortex [1]. The location of the primary gustatory cortex is not precisely known but is thought to be in the posterior insula and opercular regions near the central sulcus [3]. It is important here to outline the process of smell as this is a central subject to the subject of the supertaster phenomenon.

Non-volatile, hydrophilic molecules which have the ability to float in the air first become attached to saliva molecules [4]. The saliva which is perfused with the molecules comes into contact with papillae on the tongue and only the specific papillae that are able to sense a specific taste become enervated which causes the nerve signals to travel to the primary gustatory cortex [4]. Three types of papillae exist. First, circumvallate papillae are located at the back of the tongue and connected with the ninth cranial nerve [4]. The function of these papillae is sensitive to sensitive to sour and bitter tastes [5]. The sensory function of the glossopharyngeal nerve affects the posterior one-third of the tongue, the pharynx, and the middle ear [6], the motor function of the glossopharyngeal nerve stylopharyngeus and the autonomic function to the parotid gland [6]. A second sense is operant in the sensation of taste.

The sense of smell is an interconnected sense with the sense of taste [2]. The sense of smell operates in a similar manner as that of the sense of taste. The sense of smell involves molecules that bind to the receptors that send projections to the brain [2]. The olfactory receptors receive the same type of molecules as the gustatory receptors. The main difference between the sense of gustation and the sense of olfaction is that the sense of olfaction is not only used for sensing food but for also for sensing other animals and environmental smells such as odors which could signal danger such as smoke, or pheromones which aid in the mating patterns of animals [2]. Other functions of the insular cortex are to determine food preference, aversion against harmful foods, stimulating appetite towards beneficial foods, and personal tastes because in the evolutionary developmental sense of the human species this area of the brain was the center of food appraisal [7]. One instrumental connection with the insular cortex that establishes the connection between the sense of olfaction and the sense of gustation is that when the insular cortex is lesioned one of the results is anosmia and ageusia

also known as the loss of smell and the loss of smell respectively [7].

If we understand the function of the insular cortex, we glean the knowledge that this cortical structure is involved in sensory processing, the repression of feelings and emotions, autonomic control, motor control, risk prediction, decision making, bodily awareness, self-awareness, the fear circuit, social emotion processing acquisition of taste and taste aversion [8]. Lesions to the insula can cause changes in all of these areas, but those that deal with anosmia, ageusia, and even in some neurodegenerative diseases people will even eat putrid foods [8]. It is important to understand that certain conditions change the ability of a person to sense of either in the diminishment of sense taste either through the diminishment or enhancement of gustation or olfaction.

Several factors exist to contribute to changes in the perception of taste. Individual reasons for person-to-person variation in taste perception originate from variance of peripheral or central processing of taste sensation, subjective and environmental factors [9]. There are a number of factors that affect our taste perceptions. Yet according to Puputti, these factors are understood well as these factors are understudied [9]. What are these factors? The factors that affect taste perception include gender differences; age-related alterations; weight; food consumption customs; state of health; nervous system lesions; diseases; medication; heavy smoking; sex hormones; appetite regulation hormones; genetics; peripheral and central processing of taste transduction; the effects of saliva; density of taste buds and taste bud physiology; and alterations in brain function [9].

One criterion in which variances occur in taste perception is in the category of gender. This area of research is not well understood, yet there is clear evidence that females have better taste acuity than males [9]. These results are mixed based on the category of taste being investigated. For example, with umami taste acuity, there is no difference between males and females [9]. There are some substances that females tend to sense more strongly. These substances are PROP that is a protein involves taste receptor 2 members 38 encoded upon the TAS2R38 gene which helps to regulate the function of bitter taste receptors which are sensitive for citric acid [9]. Women also have a stronger acuity for sodium chloride as well [9]. When tested for sucrose, monopotassium glutamate, and quinapril hydrochloride which is a hydrochloride salt form of quinapril which is a non-sulfhydryl angiotensin converting enzyme inhibitor with antihypertensive mechanism [10] a different result is obtained. According to Puputti, males and females do not have any difference in acuity for these substances [9]. Even though gender differences in taste are not well understood, some theories do attempt to explain why females seem to have better taste acuity than males. One piece of evidence is that gender differences are thought to exist in the peripheral and central processing of taste perception [9]. This would suggest the validity of another line of evidence found in another study that proposed that fungiform papillae which is relative to tongue size, which is also relative to body size, result is that females would possess a higher density of fungiform papillae than males

[9]. One could extrapolate that women are known to possess the higher density of fungiform papillae would possess a higher level of acuity for the specific taste sensation.

When considering the effects of estrogen versus testosterone the first fact that must be acknowledged is the physiological gender differences in taste. First, as a consideration of females and the impact of estrogen, one way to consider this is with pregnant women who possess a greater quantity of estrogens in the body than in women who are not pregnant. During pregnancy, other sensory modalities are affected by the change in hormone levels associated with pregnancy and labor such as an increase in the pain threshold, an increase in nasal stuffiness and congestion which can alter taste perception which has the effect of altering feeding behavior and what foods a person will consume, and the anecdotal evidence that pregnant women experience hyperosmia [11]. Another set of circumstances that pregnant women are confronted with in terms of physiological alterations to the mouth such as dry mouth which can affect taste perception, differences in salivary proteins that vary with hormone levels during pregnancy, and changes in the pH and a decrease in the salivary flow rate which all have effects upon taste perception [11]. The physiology of the mother changes to support fetal development and the reception of adequate nutrition which is facilitated via taste perceptions [11]. With these physiological changes which influence some of the factors that influence taste perception, what is the result of these changes in pregnancy? The many physiological changes contribute to about 90% of women who experience alterations in taste sensation and thus one should extrapolate that physiological changes alter the taste buds and other influences in both males and females will lead to the alteration of taste perception [11]. Pregnancy is a state of being which is caused by physiological changes to the body that influence taste perception as well as giving clues as to the development of taste disorders.

Another concept that illustrates the change in the gustatory sense occurs when a person undergoes chemotherapy. Chemotherapeutic substances cause a wide range of side effects, and these side effects include taste alterations depend on many factors such as disease stage, combinations of chemotherapeutic pharmacology, and dose [12]. These taste alterations can create taste sensations that are generally unpleasant for the person undergoing cancer treatment. Approximately 75% of patients receiving chemotherapy self-report that food tastes metallic, like cardboard, like sandpaper, too salty, too sweet, too sour, too bitter, or is devoid of taste [12]. Some of these taste alterations involve either the actual taste buds or in the case that it tastes like sandpaper involves mechanoreceptors that sense textures. Such sensations cause food aversions, and these food aversions have the potential of permanently changing the very nature of the taste sensation of a person even after the cessation of chemotherapy. Taste alterations are one of the neglected conditions that cancer patients experience because taste alterations pose no risk of mortality as would vomiting and diarrhea which are known to cause taste alterations based on the occurrence of these con-

ditions [12].

Dysgeusia is a complex disorder because of the numerous ways it manifests. Dysgeusia is a disorder that is described as a change in taste sensation [13]. Chemotherapy induces symptoms such as anemia, thrombocytopenia, neutropenia, anorexia, constipation, diarrhea, mouth lesions, nausea, vomiting, pain, depression, tumor lysis syndrome, cytokine release syndrome [14]. Notably, gastrointestinal symptoms can be very problematic in the development of dysgeusia, yet other symptoms can contribute to the pathophysiological conditions that give way to the onset of dysgeusia. The altered sense of taste affects a person while eating, imbibing beverages, and even at times when a person is not engaged in eating food or drinking beverages [15]. There are specific symptoms that people complain of such as the presence of metallic tastes, bitter tastes, salty tastes, and sweet tastes that evoke an unpleasant response which impairs the enjoyment of some or all foods causing aversion [15]. The symptoms of dysgeusia here are the result of many disorders, yet in the case of people who endure chemotherapy treatments due to some forms of cancer, especially breast cancer. Breast cancer is a salient topic here because the subject of the case study involves looking at breast cancer as a likely contributor or the genesis of dysgeusia.

Any person who has experienced a common cold or even an example that is more salient of an infection from the SARS-CoV-2 virus, there is a very telltale symptom that occurs with these two viruses. Viruses from the coronaviridae family are the etiology of viral upper respiratory infections which result in secondary rhinitis leading to nasal destruction or direct viral injury of the olfactory neuroepithelium which attenuates the ability of a person to perceive the flavor of foods [16]. There is some anecdotal evidence about mild coronavirus infections. With mild infections of SARS-CoV-2, olfactory dysfunction is noted as one of the tell-tale symptoms [16]. Even with severe infections of SARS-CoV-2 that require intensive care unit admissions, the first symptom noted by patients is the discomposing of taste and flavor perceptivity in advance of the respiratory involvement [16]. As discussed earlier, factors that affect taste perception include gender differences; age-related alterations; weight; food consumption customs; state of health; nervous system lesions; diseases; medication; heavy smoking; sex hormones; appetite regulation hormones; genetics; peripheral and central processing of taste transduction; the effects of saliva; density of taste buds and taste bud physiology; and alterations in brain function [2].

The discomposing of olfaction and gustatory symptoms occurs in 65.7% of patients following ear, nose, and throat symptoms [16]. What does this mean? The change of gustatory and olfactory symptoms signal that smell and taste disorders due to the infection as an initial symptom to identify the type of infection [16]. What is the possible cause of gustatory and olfactory disruptions due to SARS-CoV-2?

In Brazil, post-mortem autopsies provided evidence based on sex differences presented with SARS-CoV-2 infections regarding the olfactory bulb. The results of the study provided that females possess more olfactory bulb neurons than

men which explain why women possess higher taste and smell acuity than men [16]. Since this fact is known about the differences in the number of olfactory bulb neurons, the study from Brazil also found that females have a greater susceptibility in the development of olfactory and gustatory sensory alterations because inflammatory cytokine production occurs more in females that cause the sensory alternations [16]. Inquiries as to the mechanism that causes olfactory and gustatory alterations with SARS-CoV-2 infection have been suggested. The mechanisms that cause the sensory alterations occur through inflammatory cytokines with infection and the spike glycoprotein which depending on the strain of SARS-CoV-2 can cause a varying dysfunction of the sensory dysfunction [16].

Other causes of hypogeusia are known. One real danger that can come about is the cleaning chemical exposure of the mouth [17]. The causes of hypogeusia are many and include the following precipitating conditions: primary medical pathologies, psychopathological causes, pharmaceutical agent side effects, chemicals, toxins, localized mouth disorders, decreased salivation, surgery, and gastroesophageal reflux, comorbid conditions like oral candidiasis, diabetes, hypothyroidism, Sjogren syndrome, and age [17]. Chemical exposures, such as ammonia and hydrocarbons produce specific lesions on the tongue of a person causing damage to the surface of the tongue [17]. Other chemicals are known to cause alterations in taste sensitivity. Chemicals such as dichromate ($Cr_2O_7^{-2}$), chromic acid (H_2CrO_4 or CrH_2O_4), and zinc chromate ($ZnCrO_4$) causes an elevation of the taste threshold when a person experiences chemical exposure to the tissue of the mouth [17].

The mechanism that causes the damage to tissues of the mouth, as well as the subsequent hypogeusia can at time be determined and at others cannot be determined. In the case of exposure to ammonia, the chemical that is responsible is urea sulfate ($CH_6N_2O_5S$) which has mild corrosive properties that area catabolized into urea (NH_2CONH_2) and sulfuric acid (H_2SO_4) containing a proprietary organic salt contacted the oral mucosa [17]. An abbreviated toxicology study was unable to determine the specific components of the cleaner, however, based on comparison to similar cleaning materials, the presumed compound was likely urea sulfate, a mildly corrosive salt that rapidly breaks down into urea and sulfuric acid [17].

Hypogeusia has specific symptoms. These symptoms help to distinguish the different taste disorders. Hypogeusia shares many symptoms with Burning Mouth Syndrome (BMS) whose characteristic symptoms are a burning sensation, tingling, or numbness without visible inflammation or lesion which affects the mucosa of the oral cavity, the lips, and the tongue [17]. Pathophysiologically, there are two factors that are associated with BMS which are angiotensin converting enzyme inhibitors or ACE inhibitors which inhibit the mechanism of action of zinc on salivary glands and the receptor cells of taste which affect taste and oral candidiasis [17]. Understanding these mechanisms of action is pivotal to the treatment of hypogeusia.

Medical treatments are available to treat hypogeusia. People who take ACE inhibitors, such as lisinopril and non-sulfhydryl which are prescribed for hypertension upon the presentation of hypogeusia would warrant discontinuation of the pharmacological agent [17]. Another therapy is to ingest selenium methionine as a dietary supplement which can help to resolve the dysgeusia [17]. If there are co-morbid conditions that present with taste alterations such as diabetes, Sjogren syndrome, hypothyroidism, and vitamin insufficiencies, these conditions should be brought under control [17].

Angiotensin-converting enzyme type 2 (ACE2) receptors allow 2019n-CoV, also known as SARS-CoV-2 or Covid-19, is the causative receptor that allows the virus to enter the cell for replication [18]. It is important to understand what cells have ACE2 receptors. ACE2 receptors are located in the following tissues: renal tissue, cardiovascular tissue and gastrointestinal tissue, lung tissue, epithelial cells in the alveoli, small intestine enterocytes, endothelial cells of the arteries and veins, and smooth muscle cells of the arteries [18]. The ACE2 receptor has specific functions in the body. When ACE2 expresses itself, the functions associated are the innate and acquired immune responses, cytokines IL-1, IL-10, IL6, and IL-8 secretion [18]. A consequence of specific viruses using the ACE2 receptor is that this receptor is thought to prolong the life cycle of the specific virus, virus replication enhancement and mediates viral access into the host cell [18]. This is very important for understanding taste disorders. The cytokines mentioned have specific functions as will be defined here and linked with how this contributes to a taste disorder.

Interleukin 1 (IL-1) is an inflammatory cytokine that causes a number of biological functions. IL-1 is involved in the body detecting cellular injury via the inflammasome [19]. The inflammatory cytokine IL-1 regulates inflammation, tissue damage, is a leukocytic pyrogen which mediates fever and acts as a leukocytic endogenous mediator, and is an inductor of some components involved in acute-phase response and lymphocyte-activating factor [19]. The involvement of IL-1 causes the initiation of the immune response yet when the immune response becomes with the high expression of IL-1, this can cause what is known as a cytokine storm which is the response of the body to mount the all-out attack to cause death to any cell or microorganism [18]. Interleukin 1 is one factor that brings about the onset of taste disorders such as those in the case of tonsillectomies where tissue injury occurs as a result of the surgical procedure which leads to the release of IL-1 and causes serum-tissue zinc redistribution resulting in the potential for a taste disorder to develop [20]. Since surgery causes a demand for zinc to cause blood clotting and wound healing, a zinc deficiency post tonsillectomy accompanying the use of analgesics and antibiotic which are zinc chelating pharmacological agents and the longer these pharmacological agents are in use with a patient, the greater likelihood that a taste disorder will develop [20]. A second factor involved in the development of taste disorders is Interleukin 6 (IL-6).

Interleukin 6 (IL-6) has a central involvement with cytokine storms in that various acute-phase proteins such as C-reactive protein, serum amyloid A, α-1 antichymotrypsin, haptoglobin, fibrinogen and the components of complement [21]. Interleukin 6 is known to initiate the coagulation cascade which is associated with disseminated intravascular coagulation onset and is a biomarker for severe clinical manifestations of an illness [21]. The connection between IL-6 and taste disorders is that it acts upon olfaction manifesting as hyposmia [21]. Since taste requires two sensory systems, what is hyposmia? Hyposmia is a medical condition in which a person either loses part or all of the sense of smell [22]. Interleukin-6 when present with pro-inflammatory cytokines such as Tumor Necrosis Factor alpha (TNF-α) in either the olfactory bulb or central nervous system (CNS) then hyposmia will be present and specific diseases that exemplify this are 1918 H1N1 influenza virus more commonly known by the misnomer Spanish Flu; 2009 H1N1 influenza virus commonly known as Swine Flu; HPAI H5N1 influenza virus known as Highly Pathogenic Avian Influenza A; and SARS-CoV-2 commonly known as Covid-19 [21].

Interleukin 8 is an inflammatory mediator factor as well as a chemotactic factor that is naturally found in mucus that originates in the olfactory tract of elderly people which contributes to a decline of olfactory sensitivity which is the causal factor of olfactory sensory decline in aging [23]. It is notable that this change happens around the fifth decade of life which causes a person to have an attenuated ability to discriminate and identify odorants as well as leading to the loss of olfactory function which is associated with neurodegenerative pathologies that occur later in life including Parkinson's Disease and Alzheimer Disease [23]. As humans age, the body is more susceptible to inflammation and the gustatory sense is one that is affected by inflammation. It is suggested that inflammation has a role in the attenuation of the olfactory sense with aging [23]. The nasal cavity and olfactory mucosa is a known anatomical location which IL-8 has important roles such as recruiting and activation of immune cells, mediates innate immunity, and when IL-8 is found in higher concentration in healthy people it is a biomarker that continuous immune surveillance and clearance through the medium of nasal mucus is indicated [23].

Interleukin 10 (IL-10) is an immunosuppressive cytokine which been shown to inhibit the ability of dendritic cells that stimulate CD4+ T-cells, to downregulate MHC-II, CD86, and presents antigen to CD4+ T-cells [22]. In what type of people does IL-10 have its biological effects? People who are considered obese (having BMI = 30 > BMI > 40) have concentrations of leptin, which provoke the production of IL-6 and TNF-α from adipose tissues as well as elevate the risk of contracting a viral infection [24]. In the nasal cavity, IL-10 deficiency in taste sensory tissues produces structural defects and the mechanism proposed that accomplishes this outcome is the elevation of inflammatory responses which curtain cell renewal as well as accelerating cell death [23]. Interleukin 10 is also linked with neurodegenerative pathology in another manner. When IL-10 circu-

lates in the blood, there is a consequential association with the protein amyloid in that IL-10 is a biomarker for amyloid deposition in the brain which leads to Alzheimer's disease along with other biomarkers [23].

These factors all contribute to the development of taste disorders in both healthy persons and people with a wide range of pathologies. There is a subsequent change of gustatory or olfactory function which causes changes in taste and smell sensitivity across a wide range of pathologies. It is also notable that certain conditions such as obesity, neurodegeneration, and other pathologies have an involved symbiotic relationship with immune responses which can exacerbate not only other pathologies, but also signs of these pathologies. As we understand the mechanisms of taste disorders and how they affect a person biologically, it is equally important to understand the psychological and social effects upon people who suffer from these complex disorders.

The olfactory and gustatory senses as mentioned previously aids us as humans as well as other living organisms to sense sources of nourishment in the environment as well as keeping the same humans and other organisms from harm. The lesson that is to be learned from this is that in the evolutionary scheme of life, humans and other organisms have evolved to first survive through olfaction and gustation to sense beneficial sources of nourishment and poisons within our midst. In a neuroethological sense, to understand how human gustation and olfaction evolved to their current state we must first take a look at mice.

Mice and their olfactory functions take on the following roles: feeding, mating, nursing their young, and avoidance [25]. In the parlance of evolutionary biology, the basic and primal motivations which are evidence of the hypothalamic function is colloquially known as the Four F's listed as following in a family-friendly manner as fighting, fleeing, feeding, and mating as well as associated activities which are mediated by the sympathetic nervous system [26]. Neurobiologically, the areas of the brain that are to be examined in this sense are the hypothalamus, the insular cortex, the reward circuit which includes limbic regions known as the ventral tegmental and nucleus accumbens as well as many more depending on the function in question [27]. This process has multiple layers. At the layer of the neuroanatomical and molecular neurobiology, we understand that the threat is detected through the senses which activate the amygdala (fear center), the amygdala projects to brain stem neurons which inhibits the parasympathetic nervous system (PNS) while simultaneously activating the sympathetic nervous system (SNS) [26]. The SNS releases cortico-releasing hormone and adrenocortical hormone to stimulate glucocorticoid secretion from the adrenal glands [26]. In what is commonly known as the fight or flight response, three responses define a response that is dependent upon a level of threat being detected and subsequently after evaluation an animal or person may choose to flee, freeze, or fight the impending danger [28].

The process of mating involves the following neurobiological process. First of all, mating is a social process that is connected with other social processes. The

choice of mates in rats, comparative to other animals including humans, possesses the characteristics of a social cognitive process requiring mechanisms for the acquisition, processing, the retention, and enactment of behavior on social information [29]. How does this process work in the sense of using the olfactory sense? Odors are a primary source of either direct or indirect social information that provides information about others and provides information for others [29]. One curious would be drawn to the next stage which is asking what is involved that the sense of smell is involved in social processes? Social and sexual behavior, as well as motivation and social cognition involve evolutionarily conserved neurotransmitters such as dopamine and serotonin in the mesolimbic reward circuit and the social behavior network as well as other neurotransmitters associated with social recognition and learning such as opioid peptide systems, testosterone and estrogens, corticosteroids, neurosteroids, oxytocin, arginine-vasopressin, and other neurohormones that are involved in reproduction, immune components, and products of the microbiome [29]. It has been established that oxytocin, which is manufactured in the posterior pituitary, contributes to parental behaviors, causes uterine contractions when a woman is in labor, and other effects as an example [26]. A second fact must be mentioned here. Oxytocin is found in high concentrations when couples post-sexual activity which causes displays of physical affection more than the norm, the strengthen of a pair bond and other effects [26]. In the area of social and psychological effects, humans operate in the same manner as rodents such as rats even as we have a more developed frontal cortex. The social and psychological effects are relatively the same and have extensively been told through the fields that deal with comparisons of both animals and humans.

2. Objectives

The objectives of this study are to put into literature this specific case of a taste disorder. The subject in the case study when faced by the general medical community finds that medical professionals in some form reject the given evidence of a taste disorder as well as its effects either through not being knowledgeable about taste disorders which need to be studied more in the nursing profession and medical community as a whole to be able to understand and deal with people who have similar experiences as the subject of the case study. Second, the medical professionals encountered by the subject of the case study have been dismissive because they do not believe such a manifestation is possible for whatever reason.

A second objective of the case study is to bring attention to taste disorders in the fields that are neuroscience adjacent as well as fields such as psychology, and medical fields that, as a norm, do not encounter neuroscientific based disorders.

The third objective is that cases like the one being presented are potentially rare or under-reported and should be brought to the attention of the body of scientific literature.

3. Methods and Materials

This study is a case study which is performed in the qualitative sense which seeks to understand the human experience of certain phenomenon.

The materials used for this study were an open-ended interview as to the manifestations of the details of the case. The interview questions and answers were spoken, and the questions were formatted in the manner of collecting information during a medical consult to ensure that a complete history and manifestation of the taste disorder is recorded accurately. Responses were recorded word for word on paper and verification of answers was conducted via reframing of ideas for the sake of brevity and for main points to highlight during the exposition of the case. History taking questions were gleaned from the following book: A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary authored by Otfried Spreen and Esther Strauss in 1991 published by Oxford University Press. The questions can be found on pages 4 to 8 in this compendium.

4. Presentation of Case

This is the case of J. M. who is female and is of the age 46 years 11 months 5 days (**Figure 1**). J. M. was born in Mexicali, Baja California, Mexico. J. M. is biological female, height 5 feet 4.5 inches (163.83 cm). She currently resides in the Cathedral City, California, United States of America. She resides with her domestic partner, has no children and has not been married. She has an active social life with many social supports and in the future seeks to further her education pursuits to a specific industry, namely cybersecurity.

In terms of education, J. M. attended the following elementary levels in Mexico: pre-kindergarten to grade 8. Subsequently, she continued her education in California from grade 8 until 12th grade attaining her high school diploma. From 1996 until 1999, she studied at College of the Desert in Palm Desert, California as a double major in Mathematics and Biology and subsequently transferred to the University of California Los Angeles (UCLA) from 1999 to 2001 where she studied biostatistics. She had to leave UCLA before her graduation to take care of her father. In the future, she plans to earn her Bachelor's degree in the field of information technology or cybersecurity. The mother language of J. M. is Spanish, yet she speaks Italian, Brazilian Portuguese, and American Sign Language.

J. M. currently works at College of the Desert as an information technology technician, a position she has held for 20 years as of November 2021. She has trained in I. T. for the past 15 years earning certificates to keep current knowledge in her field. Now for a discussion of family information, neurologically and medically relevant information, I shall mention here that some family members have personal perceptions relating to fat and obesity that are linked with the genetic portion of the discussion section. Those attitudes have been observed by this researcher to verify the validity.

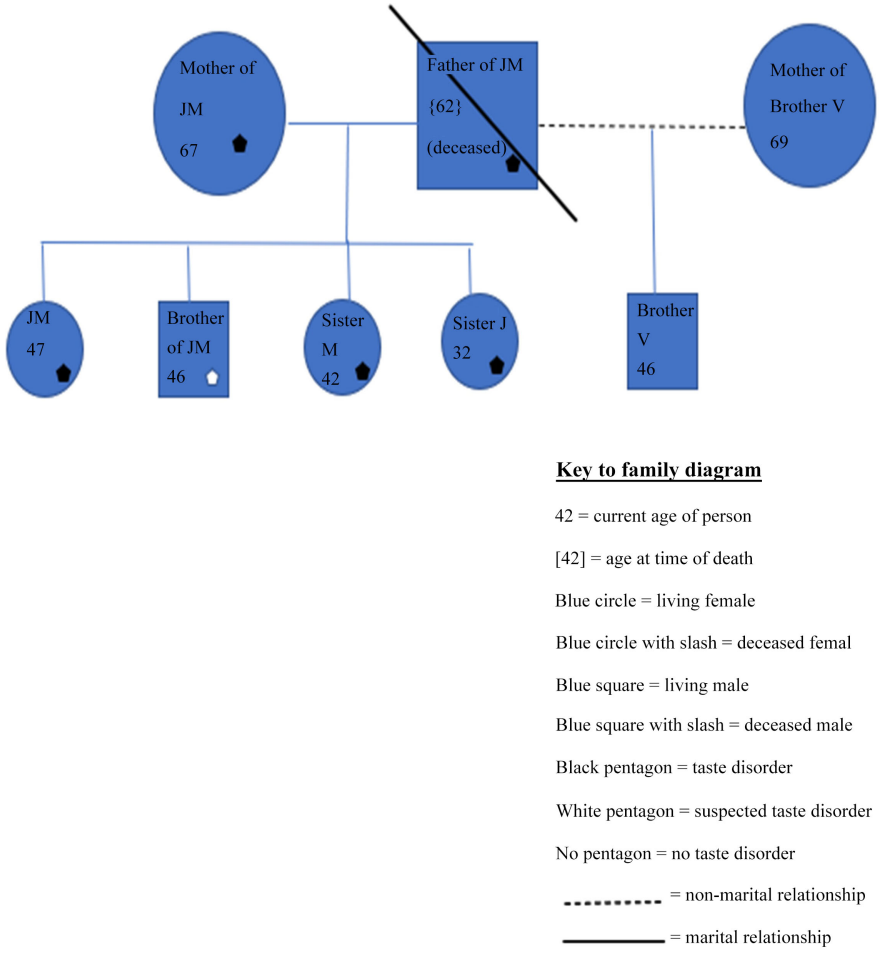

Figure 1. Familial diagram of proband J. M.

The father of J. M. was born in Atotonilco, Jalisco, Mexico. His trade was welding. He was the father of five children. During his life, medically he was diagnosed formally with diabetes type 2, hypertension, hyperlipidemia, obesity, and cardiovascular disease several strokes, a heart attack. At the age of 62 years, he died from cardiac arrest.

The mother of J. M. is currently 66 years of age. She was born in Mexicali, Baja California, Mexico and currently resides in Cathedral City California. Most recently, she had back surgery to fuse the lumbar vertebrae L4 and L5 approximately 6 months before this study. Medically, she has currently been diagnosed with diabetes type 2, hypertension, hyperlipidemia, an iron deficiency, obesity, and Bipolar Disorder type 1 with manic episodes according to the Diagnostic and Statistical Manual 5 (DSM 5). All conditions listed are controlled for by medication and other medical therapies. J. M. avoids eating vegetables, a trait she shares with her daughter whose history is given under the name Sister J. In the past, she had a cancer diagnosis with treatment course unknown. The mother of J. M. denies that anyone in her family has ever had cancer whilst evidence exists of multiple members receiving diagnosis, treatment, and only a few have succumbed to the malady. In getting to know the family, it has been noticed that the

mother of J. M. exhibits some of the same characteristics of a taste disorder, namely the elevated olfactory presentation that is present for J. M.

J. M. has two sisters, one brother and one half-brother. Of the sisters, one sister is disabled by blindness because of street drug use. The order of the sibling description shall be as follow: Sister M., Sister J., Brother R. and Brother V.

Sister M. has been involved in criminal activity due to addiction and for survival. She is known to have advanced stage rheumatoid arthritis which is speculated by family to be her entry into street drug use. She birthed one child whom she is currently estranged. Other information is not known especially if there is a taste disorder present.

Sister J. who is currently in school studying to become a nurse and works in the medical field, currently has been diagnosed with Bipolar disorder type 1 with mania according to the DSM 5 and is not controlled for by any treatment. Sister J. is married, has 5 children with plans for a sixth child, and currently lives in Cathedral City, California. Outside of obesity, there are no other medical conditions known and a taste disorder does not seem likely by long-term observation.

Brother R. currently resides in Cathedral City, California. He is the father of three children, one who is by trade a phlebotomist, one child in college, and one who he coparents with an ex-wife. His marital status is divorced and currently no in a romantic relationship. Previously, he worked as a mechanic, owned a business that did not survive its growing pains, trained as a police officer, and currently works as a personal security detail for a celebrity who shall remain unknown. No known medical information is known for Brother R. except for the medical diagnosis of diabetes type 2. He has been observed by this researcher as not having any attributes of a taste disorder over a long-term observation.

Brother V. currently lives in the State of Ohio and is married. He has retired from the military and has other employment namely his own business. No further information is known about Brother V.

J. M. is ambidextrous, yet prefers to write with her right hand. She has been diagnosed at different times with obsessive-compulsive disorder, dyslexia, anxiety disorder with hoarding, and a continuous non-clinical depressive disorder, and she suspects she has a sleep disorder that will need evaluation. She has allergies to milk (cow), wheat, bivalves, latex, polyester, and seasonal allergies. One medical professional diagnosed her with chronic fatigue syndrome which has been of controversy according to records. She had kidney stones, and surgery to remove her gall bladder, surgery for a torn meniscus due to a workplace fall which also resulted in a compression of lumbar vertebral disks at the location of L4 and L5. She did have a breast cancer diagnosis that resulted in treatment using chemotherapy which has been in remission since the cessation of therapy. The medications used for chemotherapy were not recalled and the information could be found at this time. Chemotherapy did cause some throat scarring as a result of acid reflex and vomiting. J. M. suffers from diabetes type 2 which is controlled for by medication, exercise, and diet; carpal tunnel disorder con-

trolled for by exercises; and obesity. It should be noted here that the familial and personal inclusion of obesity is included here because it could factor into taste disorder physiology and give rise to conditions which may be responsible or explain the presentation of a specific taste disorder.

In her childhood, her seasonal allergies have brought about respiratory issues such as bronchitis and pneumonia on several occasions for a period of time. At the age of 8 years and 16 years, J. M. had chickenpox. Between the ages of 11 and 12 years of age, she had gall bladder stones, mumps and gastritis, an anaphylactic exposure which resulted in loss of consciousness and required resuscitation; and hepatitis B.

J. M. currently takes the following medications, Metformin, Glyburide, Eyedrops, Lisinopril, Aldactone, Atenolol, and antihistamine. She has allergies to the following medications: cortisone, latex, and histamine. To conclude the medical history, there is no history of smoking, alcohol abuse, intravenous/street drug use, nor other neurological involvement that has been listed.

J. M. has a taste disorder. She reports that smells and tastes are more pronounced. She reports that the onset may have come shortly after the cessation of chemotherapy, but the onset could have been before this time, but the presentation of the taste disorder was not as it is today. When she noticed smells more strongly after chemotherapy, she would ask people around if they smelled what she smelled. She also used lotion on her feet and would paint her nails. She stopped this practice which caused her to stop taking care of her feet in her usual way because she would strongly sense, both her gustatory and olfactory sense, the odorants from the nail paint and the lotions. Perfumes would cause the same effect. She reports that the lotions and the flowery smelling perfumes would cause headaches and sneezing. Going into the detergent aisle would cause sneezing. Some unspecified odorants would cause a prickling sensation in her nose along with the ability to taste them. J. M. has scalded her tongue but not seriously where medical attention was required. She has also experienced scalded tongue when she was eating pineapple and also when she took a cough medicine that made her feels as if she had cracks in her mouth and the scalding tongue sensation.

J. M. reports that body smells would affect her. She provided examples to this phenomenon. When she was on a trip to Mexico, she entered a shop where a woman, who was not in the same room but one room away which also had an operating fan there, J. M reports that she asked her sister if she could smell fish when no fish was present. During the incident at some point, it was known that there was a lady in the back room who was menstruating which was the source of the odorant that J. M. could sense. Another example is that when she is in her office, when the sports teams would pass by her office, she could smell them outside. It is worthy to note that J. M. is enclosed in her office which has a window which was not open, and the athletes pass by a corridor which is outside of the building where there is adequate air supply. This researcher has witness her

smelling the outside dust blowing when there are no windows open and sometimes the observation happened at night when the blinds were closed or even in the daytime when the blinds were closed.

Another notable symptom of the taste disorder of J. M. is that when she receives injections, she has a sensation of taste from the injection. This has happened with an influenza shot which she reported a plastic taste sensation and a bitter taste sensation on the back part of her tongue. Another incident is that when she had to have surgery for a broken tooth, she was given a Novocain shot which yielded an acrid, metallic taste similar to aluminum.

J. M. relates that the olfactory and gustatory sensations do not vary and that she can even smell while having cold and nasal congestion although it is attenuated due to the physical barrier of the mucus. In relation to the five gustatory sensations, she explains that she has a sweet taste in her mouth all the time, yet she does not know if this is because of the chemotherapy-induced taste disorder or because of her type 2 diabetes. This sweet taste causes her to prefer umami and sour tastes like the tastes of hibiscus and green teas without adding a sweetener like sugar. She reports that she has pleasant and unpleasant after tastes. One pleasant after-taste she experiences is after drinking Diet Coke. This after-taste is described as over carbonated club soda. She describes the taste similar to quinine. A second pleasant after taste is when she eats wheat bread to which she is allergic she describes this as the fresh smell of cotton bedsheets being removed from the dryer and the smell of the heated metal from the dryer, which is steel although newer dryers may use different metals. In contrast, the unpleasant after tastes consist of bitter taste for her which is sensed when eating certain foods that are starting to go spoil.

J. M. reports that could smell the bodily scent of her nieces and nephews after they have occupied her home for a period of time. She has no history of hallucinations, no altered tastes except for saline. To her knowledge, she has never lost smell completely, yet has desired to because of the taste disorder. She has not experienced synesthesia according to her knowledge. She can at time remember smells associated with memories and at times can become absorbed in the memory similar to becoming absorbed in a daydream. She also reports that she can taste eyes drop medications and she has found a formulation that does not taste so strong. She reports two incidents where she could taste through her skin. The first is an incident where she could taste a foot lotion and the second incident where a person dripped some sweat onto her skin.

4.1. Discussion of Case and Conclusion

The case of J. M. provides an interesting glimpse into a taste disorder. J. M. provided as much history as possible and while it would have been helpful to know the missing information, it is sufficient to say that a conclusive diagnosis and examination of the case is producible. The discussion format will proceed as follows. First, the parental information as well as answering the question of herita-

bility of taste disorders followed by the discussion of the impacts of any diagnoses that J. M. has or presented in history. And in the final part of the discussion, there is an explanation as to the nature and using diagnostic criteria to classify and discuss any courses of treatment; a note of future directions for research and concluding remarks.

The parents of J. M. offer a fascinating insight into the presence of a taste disorder in J. M. as well as her own history. The heritability of taste disorders is not a controversial issue, but a matter of heritability. First, the mother of J. M. prefers salt tastes and uses salt on her food regularly. People who use high amounts of salt regularly may be a sign that a taste disorder is present in light of other evidence that will pique the observer to formulate the question of a person having a taste disorder. What is the explanation for heavy use of salt in the daily diet? The explanation is quite interesting and may hold the key to some current health issues of the mother of J. M. as well as hypothesized to be the cause of some of the health issues of the father of J. M. The explanation is that the heavy use of salt in the diet neutralizes the bitter taste and in fact the genetics of the TAS2R38 gene with the heterozygous alleles PAV/AVI which predispose a person to develop the super taster phenomenon [30]. Second, people with TAS2R38 gene with PAV/AVI alleles also avoid bitter tastes such as those contained in broccoli and green vegetables which protect the health of the heart are avoided thus raising the likelihood that people with this genetic presentation should be monitored for high blood pressure leading to cardiovascular disease that may result in heart attacks and/or strokes [30]. Other health conditions should be monitored such the accumulation of excessive body fat that is responsible for chronic inflammatory responses and other health issues which include diabetes, hypertension, hyperlipidemia, atherosclerotic diseases, and cancer [31]. There are other effects of the TAS2R38 gene on food selection. The three most important food selection alterations are bitter avoidance, salt preference with an emphasis on heavy daily use, and predisposition to heavy alcohol/alcoholic tendencies. It should be noted that food choices may be affected which can tip the balance of health status from healthy to disease [30]. At this moment, we can look to the father of J. M. and see that he was a heavy drinker with a preference for beer along with a penchant for sugar taste and this influence is suggestive that the father of J. M. could also present with the TAS2R38 heterozygous gene. This can also be confirmed by the fact that the mother of J. M. and Sister J present with avoidance of eating vegetables especially when they are of the green variety. Enough information is not known about Sister J to conclude the presence of taste disorder either through familial history or information provided. The presence of the TAS2R38 gene that both the mother and father are hypothesized to present may be an underlying condition in the familial genomes, thus causing a familial cluster of a taste disorder as well as influences that create for either shared or potential pathologies.

The heritability of TAS2R38 PAV/AVI polymorphism presents no controver-

sy in being heritable. In fact, some of the interesting presentation such as obesity is partially modulated by the TAS2R38 gene. Bitterness-sensing protein taste receptor type-2 member 38 (*TAS2R38*, T2R38) mediates taste perception and various physiological responses, including energy- and adiposity-related mechanisms [31]. Even as this evidence was found in the Korean population, it can be generalizable to other populations as in this case. It is easy to underscore that many of the processes associated with the TAS2R38 gene and connected physiological processes that are either within its domain of modulation or partial modulation are indeed heritable traits. Also, in answering the heritability question, in the Korean populations studied by Choi provides a TAS2R38 PAV/AVI genetic presentation not only influences food preferences, preferences for sweets, the use of bitter-tasting compounds such as alcohol and tobacco, but also influences the personal perception of fat which is held by some members of the family [31]. The exhaustive list of what is influenced by the TAS2R38 PAV/AVI genotype is not an option for presentation, but some points are made to show the breadth of the genotypical influence in domains of behavior, preference, perceptions, and physiological reactivity. All of this evidence suggests that heritability of the gene is not controversial, although many more reasons exist as well. Now, there is a discussion of the diagnostic history of J. M. in light of the taste disorder of presentation.

The subject of the study, J. M. in her diagnostic history as a child experienced seasonal allergy which has the tendency to cause a taste disorder known as hypogeusia. As we know, the physiology of taste disorders is changed by specific conditions as well as the treatments for these conditions. Noting the fact that there was respiratory involvement such as bronchitis and pneumonia, these diseases are known to affect the function of ACE2. Also, certain factors involved in the immunological response can help to the contributory onset of a taste disorder such as IL-1 and IL-6 which are common in the immune response. There could have been possible insults, although more so with the respiratory involvement from seasonal allergies. Mumps could have influenced the onset of a taste disorder in the pathophysiological manner of dysgeusia. Since the onset was noticed later than childhood, these conditions may be, at best, contributory factors. In adulthood, the food and seasonal allergies persisted. Kidney involvements may have influenced the ACE2 receptors, as well as gall bladder disease and surgery and surgery for the torn meniscus, may have contributed to taste disorder pathology through immunological pathways. However, breast cancer is known to have some effects on taste physiology, especially with the treatment via chemotherapy and radiative therapies. Chemotherapy through vomiting and acid reflux can cause damage to the taste buds and the tongue. It may also contribute through the process of activation of the immune system just as cancer causes similar activation. Chemotherapy can change the genetic code as well as irradiate the taste buds which can alter their function. The onset of the taste disorder may have happened around the time of chemotherapy treatment which is evidenced in scientific literature as a causative event. And finally, diabetes type two and

obesity are known to cause alterations in taste perception as evidenced by the literature.

4.2. Conclusions

Taste disorders affect many people in society and are defined as alterations in the way our gustatory sense operates by sensing chemicals within our environment. They can arise from many situations that people experience in life such as illness, medical treatments, chemical exposures, genetic influences, immunological involvement, and aging. Our ability to taste varies from person to person based on a variety of factors like gender, pregnancy, and more. When taste sensation lies outside of the normal variances, a taste disorder is evident. Alterations in taste sensations cause unpleasant sensations. An example of this from such the case study certain family members of J. M. experience an aversion to vegetable consumption. Such aversions are known to cause health issues such as specific cancers and other conditions.

Most often when taste disorders are mentioned, the most common thought is loss of taste. Other taste alterations exist such metallic tastes which are evident of dysgeusia. Dysgeusia is also a symptom of neurodegenerative conditions. People experience a heightened sense of taste or taste in unusual ways such as supertasters tasting saline when injected into a vein. Taste disorders have psychological and social affects that affect individuals differently.

In light of the evidence presented it can be confirmed that a taste disorder is present and namely J. M. presents with a taste alteration known as a supertaster. It is very interesting that one of the symptoms of the presentation of J. M. is being able to taste vaccines during the injection. This phenomenon needs explanation as to the physiological nature in which this occurs. So, what is the supertaster phenomenon? In short, super tasting is the ability to detect taste sensations more acutely than other people that also affect food preferences caused by an increased number of fungiform papillae [32].

Future practice directions involve more awareness of taste disorders by healthcare providers. Future research is needed in the area of taste disorders by all disciplines such as neuroscience, biomedical sciences, life sciences, and other allied sciences. In recent years more research has been devoted to tasting disorders yet more research is necessary for this area as well as the dissemination of knowledge across all relevant fields that involve the clinical treatment of people.

Acknowledgements

I would like to first acknowledge the faculty and staff at the School of Advanced Education, Research, and Accreditation for their support in my neuroscience studies. I would like to thank my thesis advisor, Dr. Nerea Castro, for all of her encouragement, aid, and for helping me along in my post-graduate journey in neuroscience. I would also like to acknowledge my life partner, Janet, for all of her support, laughter, encouragement, and our life together. I would like to ac-

knowledge my very large chosen family, who are too many to name in a short space such as this, for your love, encouragement, and shows of support either through Facebook likes, comments, or our conversations. And thank you for being patient for over a year in not hearing from me because I work too much at what I do. I also want to extend my gratitude to my professors and school-teachers, past, present, and future, for the encouragement, mentoring, and the many side lessons to encourage me throughout my lifetime to pursue science, music, and more.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] National Institutes of Health (2015, December 4). How Taste is Perceived in the Brain. National Institutes of Health (NIH). https://www.nih.gov/news-events/nih-research-matters/how-taste-perceived-brain

[2] Clark, M.A., Choi, J.H. and Douglas, M.M. (2018) Biology. 2nd Edition, Rice University, Houston.

[3] Chikazoe, J., Lee, D.H., Kriegeskorte, N. and Anderson, A.K. (2019) Distinct Representations of Basic Taste Qualities in Human Gustatory Cortex. *Nature Communications*, **10**, Article No. 1048. https://doi.org/10.1038/s41467-019-08857-z

[4] Purves, D. (2018) Neuroscience. 3rd Edition, Oxford University Press, UK.

[5] Bernays, E. (2016, April 22). Taste Bud. Encyclopedia Britannica. https://www.britannica.com/science/taste-bud#ref1012966

[6] Fuller, G. (2020) Neurological Examination Made Easy. 6th Edition, Elsevier, Amsterdam.

[7] Philippi, N., Noblet, V., Hamdaoui, M., Soulier, D., Botzung, A., Ehrhard, E., Cretin, B. and Blanc, F. (2020) The Insula, a Grey Matter of Tastes: A Volumetric MRI Study in Dementia with Lewy Bodies. *Alzheimer's Research & Therapy*, **12**, Article No. 79. https://doi.org/10.1186/s13195-020-00645-y

[8] Gogolla, N. (2017) The Insular Cortex. *Current Biology*, **27**, R580-R586. https://doi.org/10.1016/j.cub.2017.05.010

[9] Puputti, S. (2020) Individual Differences in Taste Perception: Focus on Food-Related Behavior. Ph.D. Thesis, University of Turku, Finland.

[10] PubChem. (n.d.) Quinapril Hydrochloride. https://pubchem.ncbi.nlm.nih.gov/compound/Quinapril-hydrochloride

[11] Choo, E. and Dando, R. (2017). The Impact of Pregnancy on Taste Function. *Chemical Senses*, **42**, 279-286. https://doi.org/10.1093/chemse/bjx005

[12] Campagna, S., Gonella, S., Sperlinga, R., Giuliano, P., Marchese, R., Pedersini, R., Berchialla, P. and Dimonte, V. (2018) Prevalence, Severity, and Self-Reported Characteristics of Taste Alterations in Patients Receiving Chemotherapy. *Oncology Nursing Forum*, **45**, 342-353. https://doi.org/10.1188/18.ONF.342-353

[13] McCance, K.L. and Huether, S.E. (2019) Pathophysiology: The Biologic Basis for Disease in Adults and Children. 8th Edition, Elsevier, Amsterdam.

[14] Gale, R. (2020) Management of Adverse Effects of Cancer Therapy. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/hematology-and-oncology/principles-of-cancer-therapy/management-of-adverse-effects-of-cancer-therapy

[15] Moawad, H. (2019, November 27) Do you Have a Bad Taste in Your Mouth? Very-well Health.

[16] Melley, L.E., Bress, E. and Polan, E. (2020) Hypogeusia as the Initial Presenting Symptom of COVID-19. *BMJ Case Reports*, **13**, e236080. https://doi.org/10.1136/bcr-2020-236080

[17] Jetté, M., Anderson, C. and Ramakrishnan, V. (2017) Case Report: Diagnosis of Hypogeusia after Oral Exposure to Commercial Cleaning Agent and Considerations for Clinical Taste Testing. *F1000Research*, **6**, Article No. 373. https://doi.org/10.12688/f1000research.11241.2

[18] Li, G., He, X., Zhang, L., Ran, Q., Wang, J., Xiong, A., Wu, D., Chen, F., Sun, J. and Chang, C. (2020) Assessing ACE2 Expression Patterns in Lung Tissues in the Pathogenesis of COVID-19. *Journal of Autoimmunity*, **112**, 102463. https://doi.org/10.1016/j.jaut.2020.102463

[19] Kaneko, N., Kurata, M., Yamamoto, T., Morikawa, S. and Masumoto, J. (2019) The Role of Interleukin-1 in General Pathology. *Inflammation and Regeneration*, **39**, Article No. 12. https://doi.org/10.1186/s41232-019-0101-5

[20] Temporale, H., Zub, K., Zatonski, T. and Krecicki, T. (2013) Post-Tonsillectomy Taste Disorders-Review of Literature. *Journal of Otology & Rhinology*, **2**, 3 p.

[21] Cazzolla, A.P., Lovero, R., Lo Muzio, L., Testa, N.F., Schirinzi, A., Palmieri, G., Pozzessere, P., Procacci, V., Di Comite, M., Ciavarella, D., Pepe, M., De Ruvo, C., Crincoli, V., Di Serio, F. and Santacroce, L. (2020) Taste and Smell Disorders in COVID-19 Patients: Role of Interleukin-6. *ACS Chemical Neuroscience*, **11**, 2774-2781. https://doi.org/10.1021/acschemneuro.0c00447

[22] Dresden, D. (2019, June 12) Hyposmia: Causes, Treatment, and Related Conditions. https://www.medicalnewstoday.com/articles/318461

[23] Wang, H., Jaen, C., Yoshikawa, K., Haneoka, M., Saito, N., Nakamura, J., Adappa, N.D., Cohen, N.A. and Dalton, P. (2018) Cytokine Profile in Human Olfactory Cleft Mucus and Associated Changes in Olfactory Function. bioRxiv. https://doi.org/10.1101/332395

[24] Khan, A.S., Hichami, A. and Khan, N.A. (2020) Obesity and COVID-19: Oro-Naso-Sensory perception. *Journal of Clinical Medicine*, **9**, Article No. 2158. https://doi.org/10.3390/jcm9072158

[25] Takahashi, H. and Tsuboi, A. (2017) Olfactory Avoidance Test (Mouse). *Bio-Protocol*, **7**. https://doi.org/10.21769/BioProtoc.2153

[26] Sapolsky, R. (2018) Behave: The Biology of Humans at Our Best and Worst. Penguin Books, New York.

[27] Höflich, A., Michenthaler, P., Kasper, S. and Lanzenberger, R. (2018) Circuit Mechanisms of Reward, Anhedonia, and Depression. *International Journal of Neuropsychopharmacology*, **22**, 105-118. https://doi.org/10.1093/ijnp/pyy081

[28] Roelofs, K. (2017) Freeze for Action: Neurobiological Mechanisms in Animal and Human Freezing. *Philosophical Transactions of the Royal Society B: Biological Sciences*, **372**.

[29] Kavaliers, M. and Choleris, E. (2017) Social Cognition and the Neurobiology of Rodent Mate Choice. *Integrative and Comparative Biology*, **57**, 846-856.

https://doi.org/10.1093/icb/icx042

[30] American Heart Association (2016, November 13) Inherited Taste Perceptions May Explain Why Some People Eat too Much Salt. ScienceDaily. https://www.sciencedaily.com/releases/2016/11/161113160331.htm

[31] Choi, J.-H. (2019) Variation in the TAS2R38 Bitterness Receptor Gene Was Associated with Food Consumption and Obesity Risk in Koreans. *Nutrients*, **11**, Article No. 1973. https://doi.org/10.3390/nu11091973

[32] American Society for Biochemistry and Molecular Biology (2012, Spring 6) A New Model to Understand the Supertasting Phenomenon. https://phys.org/news/2012-06-supertasting-phenomenon.html