Short Review of Current Research on the Physiology and Pathology of Olfactory Detection

Robert Henkin

Center for Molecular Nutrition and Sensory Disorders, The Taste and Smell Clinic, Washington, DC 20016, USA

*Corresponding author: Robert Henkin, Center for Molecular Nutrition and Sensory Disorders, The Taste and Smell Clinic, Washington, DC 20016, USA, Tel: 202-364-4180; E-mail: doc@tasteandsmell.com

Received date: November 10, 2015; Accepted date: March 25, 2016; Published date: March 30, 2016

Copyright: © 2016 Henkin R. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Most concepts related to physiology and pathology of olfaction has been related to abnormalities in neural function related to changes in central nervous system disorders or in disorders of olfactory nerves. While these events have been useful in understanding olfactory physiology and pathology most pathology of olfactory detection lies in problems related to olfactory receptor function not to the neural correlates per se. This brief review introduces pertinent information which relates to the role that olfactory receptors, their physiology and their pathology play in olfactory function.

Keywords: Olfaction; Olfactory receptors; Growth factors; Phosphodiesterase inhibitors; Theophylline

Introduction

Smell function involves a tripartite system involving the brain, nerves and receptors. Olfactory detection, which involves each of these systems, depends initially on the function of olfactory receptors through which the initial events in this sensory system occur. These events occur at the receptor membrane. These membrane proteins in which the receptors, ion channels and cell transponders reside comprise nearly 30% of the proteins in eukaryotic cells. They also constitute more than 50% of all cellular drug targets. It is the purpose of this review to discuss sensory function of the olfactory receptors, particularly in relationship to the pathology encountered in human loss of smell function, and its subsequent treatment to restore this function through specific drug effects. The changes observed by these pathological events lend insight into the physiology of olfactory detection.

Olfactory Receptor Function

Olfactory receptors have been studied anatomically and physiologically for many years [1] and are involved in the initial coding in the olfactory system [2]. These receptors are unique in that they have no blood vessels, no lymphatics, do not exhibit mitosis but turnover structurally rapidly, many over a 24-hour period, some in a few days and others in less than a month [3]. This rapid turnover depends upon the continual stimulation of stem cells in both olfactory epithelium (and in taste buds) with growth or transcription factors that stimulate these stem cells to induce the growth, maturation and perpetuation of the panoply of receptor cells necessary for receptor function in smell (and taste) [4]. Any interference with secretion of these growth or transcription factors inhibits smell (and taste) function. These growth or transcription factors comprise multiple chemical moieties but major among these are sonic hedgehog (Shh) [5] and carbonic anhydrase (CA) VI [6]; cAMP and cGMP are also important moieties in receptor function in several ways [7,8]. Each of these factors play multiple roles in receptor function with secretion of each factor enhanced by phosphodiesterase (PDE) administration [3].

Olfactory Receptor Growth Factors

There is multiple growth and transcription factors that play a role in olfactory receptor function [4]. However, there are several of these factors that play dominant roles. It is important to recognize the multiple roles each of these moieties play in receptor function both individually and together. cAMP and cGMP are the final activating steps after the binding of sensory stimuli to G-protein coupled receptors (GPCR) at the cellular membrane followed by the subsequent stimulation of adenylyl cyclase III with its downstream products cAMP and cGMP responsible for amplification of the receptor generator potential to induce depolarization and subsequent initiation of the neural response initiated at the receptor with subsequent transmission of this signal along the sensory nerves to the brain [9]. The binding of the olfactory stimulus to the GPCR activates, via the G-protein Golf, adenylyl cyclase resulting in an increase in cAMP which elicits opening of cation channels directly gated by cAMP. This induces an increase in intracellular Ca+ concentration which activates a Cl- current which, owing to an elevated reversed potential for Cl-, induces depolarization of the olfactory neurons. Amplification of the receptor generated potential leads to the subsequent generation of the action potential which conveys the chemosensory information along the olfactory fila into the olfactory bulb and ultimately to the brain [9]. This olfactory signal transduction pathway is modulated by cGMP which plays an important role in regulating function of olfactory signaling [10-13] as does calcium itself [14]. Any interference with CAMP and cGMP presence inhibits activation of the receptor signal with inhibition of smell function [3]. Both moieties may also play a role in stem cell stimulation and act as second messengers in receptor growth and development. The PDE inhibitor theophylline increases both CAMP and cGMP in patients with loss of smell (hyposmia) which activates this system and thereby improves hyposmia [1,15]. These results emphasize the role of Ca2+-calmodulin-dependent phosphodiesterase localized to olfactory cilia in this system [14,16].
Sonic hedgehog (Shh) is a major stimulator of stem cells of sensory receptors of both modalities. It has been shown to induce taste bud growth and function in animal studies [5]. Its absence increases abnormalities in taste bud anatomy and function which is corrected by administration of Shh. Thus, elimination of Shh has been shown to inhibit taste bud growth and function and taste inhibition in animal studies. The inhibition of Shh secretion of hyposmic patients associated with their hyposmia and its resecretion after theophylline treatment indicates, by analogy, that it is a major factor in growth and maturation of olfactory receptors [5].

Carbonic anhydrase (CA) VI: Theophylline stimulates secretion of CA VI in serum and erythrocytes and enhances activity of CA I, II and CA VI. CA VI, the only secreted CA, has been shown to act as both a ability to detect, and thereby lost ability to recognize olfactory stimuli, which through the action of various pathologies which interfere with mechanism(s) of action on receptor function is complex much is

Still another major cause of loss of olfactory receptor function relates to inhibition of secretion of adenyl cyclase and its downstream components cAMP and cGMP. Inhibition of secretion of these moieties causes loss of olfactory receptor function with subsequent loss of smell function [3]. Treatment with PDE inhibitors, particularly theophylline either orally or intranasally, activates secretion of cAMP and cGMP and thereby increases both receptor function and ability to detect olfactory signals [1,10].

Conclusion

These pathological events affecting smell function in humans have their action mainly by inhibition of olfactory receptor function through inhibition of secretion of these well-known growth factors which directly stimulate stem cell function to enhance growth, development and perpetuation of the elegant repertoire which comprises olfactory receptors and thereby their function.

It is through these pathological events that several important aspects of the physiology of olfactory receptor function can be elucidated.

References


