شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

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INTRODUCTION

The special sense of olfaction has always provided all different species with vital information about their surrounding environment. Being considered a ‘‘chemical sense’’ due to its capability of detecting chemical stimuli and encoding them into neural impulses, this special sensory system supplies essential information concerning environmental dangers, for example spoiled foods and fires ***(Cantone et al., 2017).***

Although humans have become more visually dominant in present time, the special sense of smell remains important. For some particular occupations - such as chefs, natural gas workers and firefighters, this sense is of utmost importance. Just importantly, this chemical sense contributes significantly to the quality of life, with devastating effects whenever lost or diminished ***(Hadley et al., 2004).***

Olfaction starts peripherally at the olfactory epithelium present in the nasal cavity, which relays sensory information to the higher cortical centres via the olfactory nerves ***(Firestein, 2001; Figueres-Oñate et al., 2014***).

Olfactory epithelium occupies the olfactory region of the nasal cavity, extending for an area of around 5 cm^2 over the nasal septum, the superior concha and the lateral wall above it. It’s yellowish in colour and thicker than the rest of the nasal mucosa (***Standring, 2015***).

Olfactory disorders lead to a decreased quality of life - in the form of mood changes and depression observed in affected patients ***(Nordin and Brämerson, 2008***), and reaching to increased mortality risks ***(Gopinath et al., 2012).***

In the most recent pandemic of Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), the causative agent of 2019 Corona virus disease (COVID- 19), olfactory loss (anosmia) has been the main neurological symptom and among the earliest reported complaints in positive cases. This lead the Centers for Disease Control and Prevention (CDC) to include sudden-onset anosmia as one of the diagnostic criteria for case identification ***(Whitcroft and Hummel, 2020).***

The power of olfaction is affected by several factors. Age and gender are two such factors with an undeniably important impact ***(Brand and Millot, 2001).***

Senile people are men and women aged 65 years and over, as is currently described by United Nations (UN) in its demographic projections ***(United Nations, 2019)***.

Histological studies of the olfactory neuroepithelium in humans and laboratory animals have proved that age-related degenerative changes do occur ***(Holbrook et al., 2005).*** Clinically, the prevalence of olfactory problems increases with age ***(Hoffman et al., 1998).***

Gender is a term that refers to “the characteristics of women and men that are socially constructed” (***World Health***

Organization, 2019). It is considered a cross-cutting determinant of active ageing as it influences all the other determinants (***World Health Organization, 2001***).

Studying the biology of gender differences is most compelling nowadays, as there is a prominent variability in human illness that has no current explanation. Being of either gender is an important basic human factor that influences both health and disease across the life span (***Wizemann and Pardue, 2001***).

Although sex differences in olfactory abilities are a well-documented clinical observation in the senile population (***Doty and Cameron, 2009***), very little attention has been paid by scientists to the intentional study of these sex differences at the fundamental molecular and cellular levels. Wherever data are obtainable, they have usually been a byproduct of other research areas. For quite a long time, researchers had assumed that no such differences existed, or were relevant at best, elsewhere than in the reproductive system (***Wizemann and Pardue, 2001***).

Among the different laboratory rodents, Syrian hamsters (*Mesocricetus auratus*) are the preferred species employed in ageing research. This is due to their possessing of several advantages over other rodents; available life table data, a short life span and a unique stability of their cells in tissue culture against spontaneous transformation into permanent cell lineages (***Masoro, 1990***).

Aim of the Work

This study was conducted to observe and describe age-related changes in the histology of Syrian hamster olfactory epithelium. It also aimed to describe discrepancies in these changes, if any were present, between both genders in this matter.

REVIEW OF LITERATURE

Anatomy of the human olfactory epithelium

Olfactory mucosa is one of five physiologically and morphologically distinct mucosae lining mammalian nasal airways; respiratory, olfactory, transitional, squamous and lymphoepithelial ***(Harkema et al., 2006)***.

It occupies the olfactory region of the nasal cavity, covering an area of around 5 cm^2. Areas covered include the olfactory cleft or groove (nasal roof), the superior nasal concha, the sphenoethmoidal recess and the superior part of the perpendicular plate of the ethmoid laterally, and the corresponding nasal septum medially. It also shares the middle concha with the respiratory epithelium in a chessboard fashion ***(Standring, 2015)***.

The olfactory mucosa is of a thicker texture and lighter colour (yellowish-brown) than the remainder of the nasal mucosa (pink) which is of the respiratory type (**Fig. I**), being of a pigmented pseudostratified epithelial type (***Sinnatamby, 2011***).

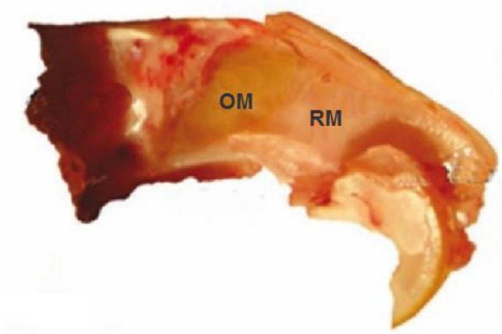

Fig (I): Nasal septum in a rat showing the location of olfactory mucosa (**OM**). The yellow colour of mucosa is evident, as is the line of demarcation between it and the respiratory mucosa (**RM**) ***(Tharion et al., 2011***).

Three recognized cell lineages are found in the olfactory epithelium; olfactory receptor cells (ORCs), sustentacular cells (SCs) and basal cells (BCs) (***Standring, 2015***).

Olfactory nerves are formed of bundles of special afferent (SA) neuronal axons, whose peripheral processes are the olfactory mucosal receptors. The axons are non-myelinated and in different stages of maturity, demonstrating the continuous turnover of olfactory receptor cells that occurs in the epithelium. The bundles unite into approximately 20 branches that traverse the cribriform plate to terminally synapse in the olfactory bulb (OB) (***Barral and Croibier, 2009***).

The aforementioned bundles are surrounded by olfactory ensheathing cells (OECs) to form a laced network in the mucosal lamina propria (**Fig. II**), whereas the branches are ensheathed by pia-arachnoid and dura maters as they cross the cribriform plate. The dura mater is continuous with the nasal periosteum, whereas the pia-arachnoid mingles with connective tissue sheaths that surround the nerve bundles; an architecture that may favour the advancement of an infection from the nasal cavity into the cranial cavity ***(Standring, 2015***).

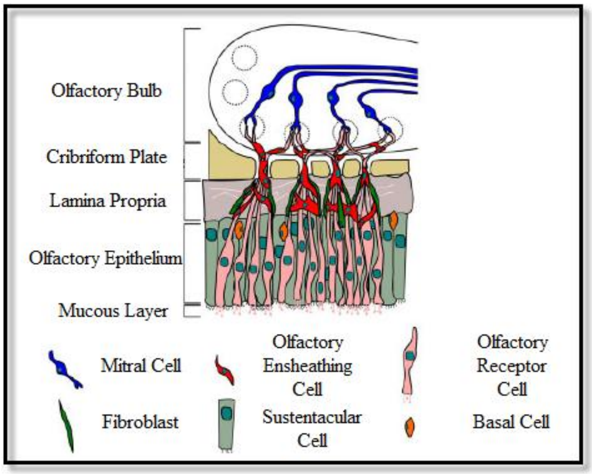

Fig (II): Olfactory receptor cells project axons to terminate and synapse in the olfactory bulb of the forebrain. The axons are seen surrounded by olfactory ensheathing cells as they traverse the cribriform plate of ethmoid bone (***Wright et al., 2018***).

In serious injuries of the anterior cranial fossa, tears in olfactory nerves or avulsion of the olfactory bulb may occur, either way leading to anosmia; loss of the olfactory sense. Fractures may also affect the meninges, leading to cerebrospinal rhinorrhea; leakage of cerebrospinal fluid (CSF) into the nose (***Standring, 2015***).

Histology of the human olfactory epithelium

Olfactory mucosa is a highly specialized mucous membrane that serves as the primary gate for the olfactory pathway. It comprises three main components; an epithelium, a basement membrane, and lastly, a lamina propria (***Chen et al., 2014***).

It is lined by olfactory epithelium – an exceptionally thick (75-150 µm in height) pseudostratified epithelium which normally consists of three cell lineages: olfactory, sustentacular (or supporting) cells and basal cells (***Young et al., 2006***).

Olfactory receptor cells (ORCs) are about 10-20 x 10^6 true slim bipolar neurons. They are formed of nucleated cell bodies - the nuclei of which inhabit middle to deep strata of the epithelium, apical dendrites and basal axons (***Dennis et al., 2015***).

The apical dendrites dilate near their end into bulbous olfactory knobs, bearing around eight to twenty, 30-200 µm long cilia (***Young et al., 2006***). Odorant receptors - transmembrane proteins responsible for detecting inhaled odorants - are located on the distal aspect of cilia (***Dennis et al., 2015***).

Olfactory cilia differ from respiratory cilia in being immotile, longer and of a characteristic tapered appearance. From each ORC base, a single non-myelinated axon emerges and pierces the epithelial basement membrane to join fellow axons from other receptor cells, eventually forming the olfactory nerve fascicles (***Young et al., 2006***).

ORCs are peculiar in several matters. They are the only sensory neurons in the human body with direct exposure to the body surface. They are also the only neurons in the body - along with the hippocampus - that are capable of regeneration (***Junqueira and Carneiro, 2005; Chen et al., 2014)***.

Moreover, ORCs are the only sensory neurons to reach the forebrain directly without synapsing first in the thalamus (***Dennis et al., 2015***).

Furthermore, the odorant receptors mentioned earlier are encoded by the largest known gene family in all multicellular organisms - human species included (***Glusman et al., 2001; Mombaerts, 2001***).

More abundant nuclei interspersed within the superficial stratum of the epithelium belong to supporting or sustentacular cells (SCs). These are elongated cells with tapering bases resting on the basement membrane. Their superficial surface bears numerous long microvilli that intermingle with the olfactory cilia, giving the characteristic striated appearance of the olfactory mucosal surface. In addition to the structural support that SCs provide, they also help phagocytose excess odiferous molecules and maintain a stable ionic environment for the olfactory cilia via H+ balance and K+ transport (***Young et al., 2006***).

A light yellow pigment is found in the cytoplasm of these sustentacular cells and is responsible for the characteristic colour of the olfactory epithelium (***Junqueira and Carneiro, 2005***).

Most recently, and surprisingly indeed, sustentacular cells were found to express the receptor proteins to which SARS-CoV-2 binds in order to enter the human cells. This contradicted the assumption that ORCs were the targeted cells and the most vulnerable among the olfactory epithelial cells (***Brann et al., 2020***).

A single file of small rounded nuclei lying along the well-defined basement membrane belong to basal cells (BCs), which are conical cells that seem to serve as stem cells for neurogenesis of the other cell lines throughout the course of life (***Young et al., 2006***).

It is truly difficult, in a standard histological section, to discern individual cell lines of the olfactory epithelium, nevertheless, the shape and location that the nuclei assume may help in this dilemma (***Eroschenko and Fiore, 2013***).

The epithelium is covered by a layer of lipid-rich mucous ~ 60 μm in thickness. The mucous protects the epithelium against turbulent airflow and desiccation, and also helps in presenting odiferous substances to ORCs via binding them to chaperone proteins (***Young et al., 2006***).

The lamina propria is a loose connective tissue rich in thin-walled blood vessels, myelinated nerve fascicles, lymphoid tissue, stem cells and Bowman's glands (***Chen et al., 2014***).

Bowman's glands are branched tubuloacinar serous glands first described by Todd and Bowman in 1847 and later named after the latter by von Kölliker in 1858 (***Dennis et al., 2015***).

Another cell type present in the olfactory mucosa is that of the olfactory ensheathing cells (OECs). These are atypical glial cells; they uniquely migrate to the central nervous system from the peripheral nervous system (***Grosu-Bularda et al., 2015; Jiang et al., 2017)***. Mature OECs are fusiform in shape, with their perikarya surrounding the olfactory nerve bundles throughout their course from ORCs to the OB (***Chen et al., 2014***).

Comparative Histoanatomy of Human and Hamster Olfactory Epithelia

Nasal cavities are generally similar in most mammalian species; however, some discrepancies are noted among them regarding the nasal architecture (***Proctor and Chang, 1983***).

Unlike rodents that have a more complicated nasal structure which serves primarily as an olfactory organ (macrosmatic), humans have a simpler nose that serves primarily for breathing (microsmatic) (***Craven et al., 2010***).

An evident difference among mammalian species is that of airflow patterns, which is mainly attributed to the complexity of branching and folding observed in laboratory rodents in contrast to the simplicity of those in humans (**Fig. III**). The shape of conchae is believed to have been affected by developmental forces concerned mainly with olfaction, as is the case with the type and dispersal of cells lining these structures (***Harkema et al., 2006***).

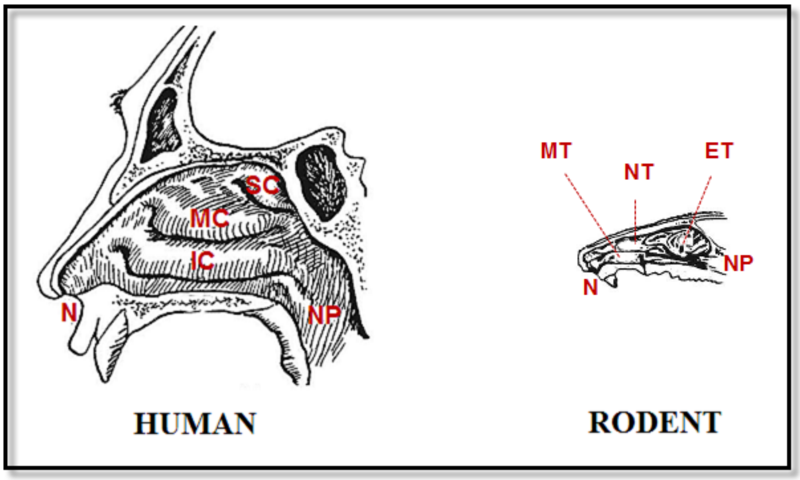

Fig (III): Diagrammatic drawing of the lateral nasal wall demonstrating the difference between human and rodent nasal cavities. **SC:** Superior Concha; **MC:** Middle Concha, **IC:** Inferior Concha, **NP:** Nasopharynx, **N:** Nostril; **ET:** Ethmoturbinate; **NT:** Nasoturbinate; **MT:** Maxilloturbinate (***Harkema et al., 2006***).

A feature peculiar of the nasal conchae and septum in humans –and some other primates- is the presence of olfactory pits, which are invaginations of the olfactory epithelium (OE) first described by ***Feng et al. (1997)***. These pits seem to enhance the surface area for olfactory reception and might as