

Olfactory Impairment in Obese Patients

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Abstract

Background: Recently published work and emerging research efforts have suggested that the olfactory system abilities is intimately affected by morbid obesity. Morbidly obese patients demonstrate altered olfactory acuity. High body mass index (BMI) appears to be associated with olfactory dysfunction. Increasing BMI may be a risk factor for olfactory loss or lack of olfactory recovery after an inciting event.

Objective: This study aimed to discuss olfactory impairment in obese patients and to elucidate what role olfactory loss may play in diet and feeding habits of obese patients

Conclusion: Our study presented a strong evidence for a causal relationship between changes in olfactory abilities of obese patients. There was altered olfactory acuity and cardiovascular, inflammatory, and cognitive declines. It was found that consumption of diets high in fat are found to cause nervous system dysfunction.

Keywords: Obesity, Olfactory, BMI.

INTRODUCTION

Our sensory systems have developed to allow us to identify, evaluate, and predict stimuli in the environment such that we make sensible decisions about them⁽¹⁾. The sense of smell is one of the most important sense for human quality of life, health, and survival. Indeed, the role of olfaction is to guide our attention towards hazards (e.g. microbial threats and poisonous fumes) or conversely, towards items with positive connotations (e.g. nutritious food). This guidance is predominantly driven by the ecological valence (pleasantness/unpleasantness) of the odorous items (e.g., food), which to a large part is determined by the individual's personal history with that item. Olfaction plays a major role in our interaction with the environment. The olfactory system not only acts for the detection of potential dangers in the environment, such as smoke, gas or dusts but also it influences our nutrition, social behavior, and well-being⁽²⁾.

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. People are generally considered obese when their BMI (a measurement obtained by dividing a person's weight by the square of the person's height) is over 30 kg/m², with the range 25–30 kg/m² defined as overweight⁽³⁾. Obesity is important risk factor for many chronic physical and mental illnesses that people suffer from. The generally accepted view is that overweight causes health problems similar to that of obesity but to a lesser degree⁽⁴⁾. Obesity impacts sensory systems, because olfaction is linked with ingestive behavior as to guide for food

choice. A number of studies have suggested that smell and taste capacity are also modulated by the endocrine system apart from central regulation⁽⁵⁾.

Morbidly obese individuals were found to have lower smell capacity than moderately obese individuals⁽⁶⁾, especially in odor detection and identification⁽⁷⁾. A number of studies have shown that not only circulating ghrelin, peptide YY (PYY) and cholecystokinin (CCK) levels are decreased in human obesity⁽⁸⁾ but also that morbidly obese individuals have lower smell capacity than moderately obese individuals⁽⁶⁾ and that impairment in odor detection and identification also exists in overweight individuals⁽⁷⁾.

Nicolas et al. reported marked loss of olfactory sensory neurons and their axonal projections after exposure to a fatty diet, with a concomitant reduction in electro-olfactogram amplitude. Loss of olfactory neurons and associated circuitry is linked to changes in neuronal proliferation and normal apoptotic cycles⁽⁹⁾. Other studies have reported that olfaction may be desensitized in individuals who are morbidly obese⁽⁶⁾. This may be due to changes in olfactory sensory neurons (OSNs). Decline of OSNs is shown to occur over time during high-fat intake in animal studies⁽¹⁰⁾.

Anatomy of the olfactory nervous system

The major components of the olfactory system consist of the olfactory neuroepithelium (OE), the primary olfactory area, the olfactory bulb (OB) and its cortical projections that is considered as secondary olfactory network areas or olfactory cortex [Fig.1]⁽¹¹⁾.

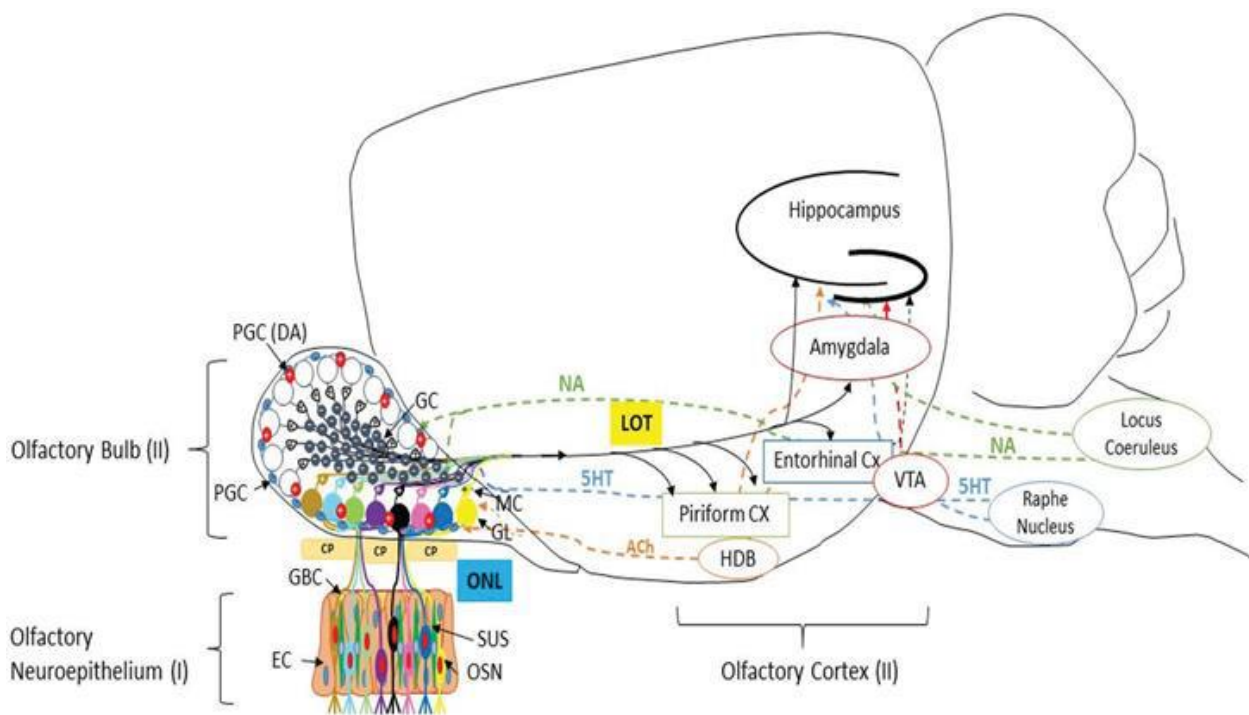


Fig. (1): Olfactory system anatomy in the mammalian brain

The olfactory epithelium is a thin, pink-to-red colored epithelium that lines the upper nasal cavities. It is situated in the superior aspect of the nasal vault in the cribriform plate medial to the middle turbinate. Some areas of the olfactory epithelium are also present in the superior turbinate, the dorsoposterior region of the septum and the anterior and middle parts of the middle turbinate. The olfactory receptor neurons are a collection of about 6 million bipolar receptor cells whose cell bodies, dendrites and initial axon segments are located within the olfactory neuroepithelium ⁽¹²⁾. Odorants reaching the olfactory cleft are probably carried through the mucus layer by olfactory binding proteins and bind to olfactory receptors located at the ORNs' cilia ⁽¹³⁾.

The olfactory bulbs (OB): It is ovoid in shape and located in the anterior cranial fossa, above the cribriform plate of the ethmoid bone, under the frontal lobe. It receives axons from the olfactory receptor neurons (ORNs), which pass through the cribriform plate of the ethmoid bone and converge into the olfactory nerves, which are surrounded by glial cells (called olfactory ensheathing cells) and project directly to the ipsilateral OB ⁽¹⁴⁾. Anatomically defined on the basis of cell type and composed of: (1) The olfactory nerve layer that is made up of axons of the incoming ORNs, (2) The glomerular layer that is composed by glomeruli where axons of ORNs synapse with dendrites of mitral cells, periglomerular and tufted cells, (3) The external plexiform layer that consists mainly of dendrites of mitral and tufted cells. Mitral and tufted cells

extend secondary dendrites into this layer, where they synapse with local interneurons (juxtglomerular, periglomerular and granule cells), (4) The mitral cells layer that contains cell bodies of mitral cells (second order olfactory neurons), (5) The internal plexiform layer and (6) The granule cell layer that contains soma of the granule cells, which represent the most numerous cells in the OB ⁽¹⁵⁾.

The olfactory tract: It is a thin, triangular, myelinated nervous projection. It originates in the anterior cranial fossa and ends in the middle fossa to give rise to the olfactory trigone ⁽¹⁶⁾, which is a widening of the olfactory tract that tends to become triangular dividing and giving rise to two main olfactory striata (lateral and medial) and a small central olfactory stria, which eventually target higher brain regions ⁽¹⁷⁾.

The main central cortical structures of olfaction include the primary olfactory cortex, the anterior olfactory nucleus, the olfactory tubercle, the amygdaloid complex and the entorhinal cortex ⁽¹⁸⁾.

Secondary central structures of olfaction include the hippocampus, hypothalamus, thalamus, orbitofrontal cortex, and cerebellum ⁽¹²⁾.

Physiology of the olfactory nervous system

Volatile chemicals enter the nose where they may activate cells of the olfactory nerve and/or free nerve endings from the ophthalmic and maxillary divisions of the trigeminal nerve. The latter nerve filaments are distributed throughout the nasal mucosa, including the olfactory neuroepithelium.

Some inhaled chemicals also stimulate free nerve endings within the oropharynx and oral cavity, such as those from the glossopharyngeal and vagus nerves ⁽¹⁹⁾.

The axons of the olfactory sensory neurons from the nasal cavity send information to second-order neurons in the olfactory bulb, which in turn project to the olfactory cortex and then to other brain areas. In addition, in the olfactory system the signals from primary sensory receptors to higher processing regions are predominantly sent ipsilaterally, rather than having a contralateral representation as the other senses. This fact allows the assessment of the relative contribution of each hemisphere to the processing of olfactory stimuli ⁽²⁰⁾.

Classification and testing of Olfactory

Disorders

Olfactory disorders are transient or permanent alterations of smell. We traditionally use different types of classifications; quantitative and qualitative ⁽²¹⁾.

Quantitative Smell Disorders:

Anosmia: absence of smell function, **Hyposmia:** decreased sensitivity to odorants, **Partial anosmia:** ability to perceive some but not all odorants, **Hyperosmia:** abnormally acute smell function and **Presbyosmia:** reduced ability to smell with increasing age ⁽²¹⁾.

Qualitative Smell Disorders:

Which are termed dysosmia (distorted odor perception or difficulty with odor identification). Dysosmia is divided into **Parosmia:** distorted perception of an odour stimulus in the presence of an odour, **Euosmia:** form of Parosmia with the distortion is pleasant, **Troposmia:** form of Parosmia with the distortion is an unpleasant. **Phantosmia:** "olfactory hallucination", an odour is perceived in the absence of any external stimulus ⁽²²⁾. Phantosmia can be divided into two types; 1st type is perceived as the odour of chemicals, animals or other person, it does not fatigue and can continue for months. In psychological disease it is always continuous. 2nd type is intrinsic: the odour seems to come from the patient himself, the odour of sweat, intestinal winds or breath. Intrinsic hallucination are dominant in patient's mind ⁽²³⁾.

It occurs as a manifestation of olfactory reference syndrome in which the patient suffers from a highly exaggerated concern affects the lives of (0.5-1%) young age that is more common in single male ⁽²⁴⁾ and **Cacosmia:** form of Phantosmia

with a bad smell. It is the perception of an odor which usually is unpleasant without an odorant stimulus, or an unpleasant phantosmia lasting only a few seconds ⁽²⁵⁾.

When assessing patients with chemosensory impairment, one should bear in mind the close association of smell and taste, where a patient complains of reduced or dysfunctional taste, often they are in fact suffering from olfactory impairment and describing consequent impact on flavor perception. For example, the patient may be complaining of retronasal olfactory dysfunction but unaware that they are also experiencing orthonasal impairment ⁽²⁶⁾.

The method used for assessing olfactory function and dysfunction is vitally important with respect to accurate diagnosis, outcome reporting and tracking of olfactory changes over time. In general, three different types of olfactory testing can be undertaken ⁽²⁷⁾:

1. Subjective, patient reported olfactory assessment using visual analogue scales, or questionnaires, which assesses overall disease burden.
2. Psychophysical olfactory assessment: The **psychophysical** tests include investigation of odor detection threshold, odor discrimination and identification e.g. (UPSIT, CC-SIT & Sniffin' Sticks). The outcome of the test is dependent on the patients' response.
3. Olfactory assessment using **electrophysiological** e.g. (EEG & EOG) which utilizes changes in cerebral blood flow in order to map brain activity changes in response to stimuli. **Radioactive isotopes** as positron emission tomography (PET) makes this a less attractive technique. Functional magnetic resonance imaging (fMRI) has become more common as well as **radiological studies** e.g. Sinus CT, MRI & FMRI ⁽²⁷⁾.

Impact of Olfactory Disorders on Quality of Life

The general role of olfaction is to guide our attention towards hazards (e.g., microbial threats and poisonous fumes) and towards items with positive connotations (e.g., nutritious food). This guidance is predominantly driven by the valence (pleasantness/unpleasantness) of the odorous item (e.g. food), which to a large extent is determined by the individual's personal history with that item ⁽²⁸⁾. Smell loss may have adverse effects on general quality of life (QoL) and can lead to depression, feelings of vulnerability, altered food intake, reduced social interaction and decreased intimacy with partner (Fig. 2) ⁽¹⁾.

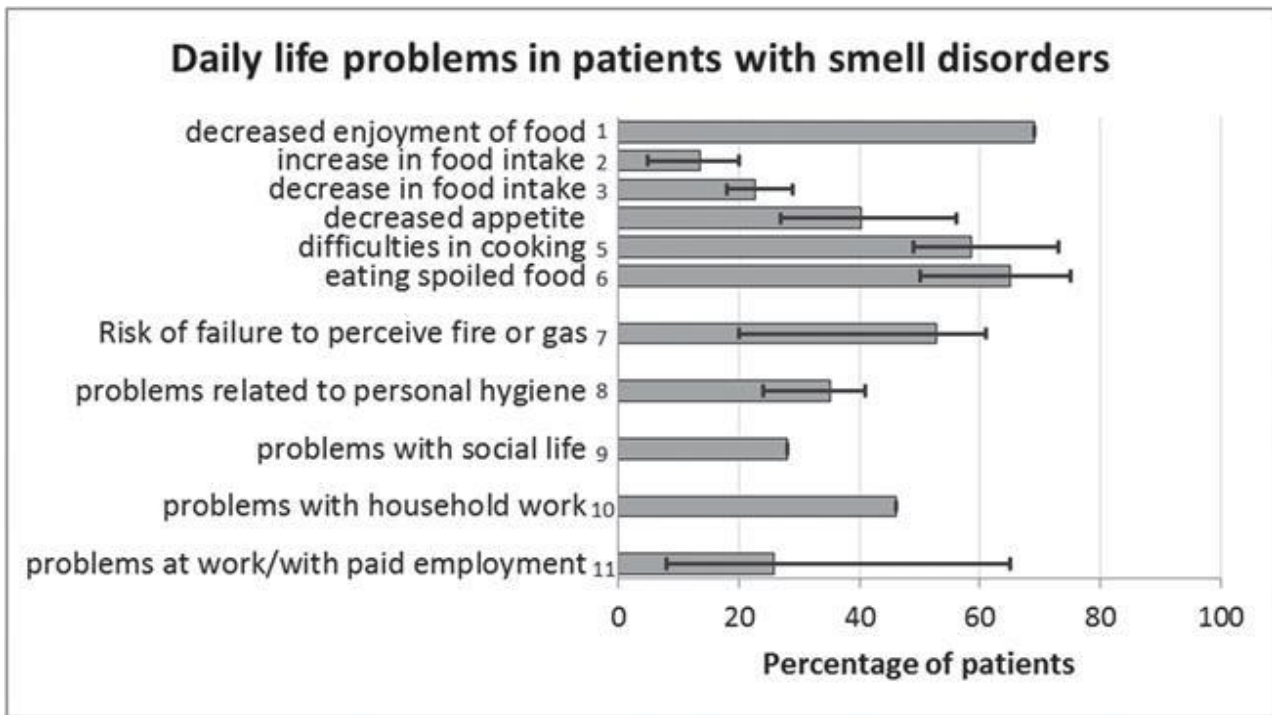


Fig. (2): Daily life problems in patients with smell disorders ⁽²⁹⁾.

Olfactory impairment with obesity

Morbidly obese patients demonstrate altered olfactory acuity. High BMI appears to be associated with olfactory dysfunction. Increasing BMI may be a risk factor for olfactory loss or lack of olfactory recovery after an inciting event and to elucidate what role olfactory loss may play in diet and feeding habits of obese patients ⁽¹⁾. Morbidly obese individuals were found to have lower smell capacity than moderately obese individuals ⁽⁶⁾ especially in odor detection and identification ⁽⁷⁾. Regarding taste, in obese adults, an impaired capacity for sweet and salty food was found ⁽³⁰⁾.

Olfactory receptor neurons showed responsiveness to the starvation signal peptide adiponectin. Also, animal models showed increased olfactory acuity in a starvation or fasting state. Human experiments showed that physiologic mechanisms acquired by this association of odor and taste when trained in a hungry state were not expressed when there is increasing BMI. The physiologic mechanism of sensory-specific satiety refers to the reduction in pleasantness of a consumed food relative to other foods and appears to play an important role in the normal decision to stop eating ⁽³¹⁾.

A number of studies have suggested that olfaction was clearly impaired in obese participants (namely in threshold & identification) and in anorexia nervosa (AN). Accordingly, while the prevalence of hyposmia in obesity was 54.3 %, in AN it was only 6.4 %. This is also the case of the sensorial system and its association with appetite, food preferences, and food intake ⁽³²⁾. However, loss

of smell (anosmia/hyposmia) and taste (ageusia/hypogeusia) are strongly associated with changes in the hedonic response to food and in weight ⁽³³⁾.

A number of studies have suggested that smell and taste capacity are also modulated by the endocrine system apart from central regulation. Several gut hormones have been linked to the smell–taste capacity with ghrelin, peptide YY (PYY), and cholecystinin (CCK) being the most representative. Thus, ghrelin seems to increase human sniffing response, peptide YY to modulate taste responsiveness, and CCK is a major agent in taste signaling. Therefore, there was interactions between gut hormones, sensory processing (taste and olfaction) and emotional regulation ⁽³⁴⁾.

Specifically, ghrelin an appetite stimulating hormone produced primarily by the stomach, induces hunger, stimulates food intake, and enhances the pleasantness of meals. It was significantly decreased in obese subjects and was related to smell impairment. Smell capacity and ghrelin may act as moderators of emotional eating and BMI. Low smell function is associated with emotional eating with the consequent increase in BMI, as found in obese patients. Decreased concentration of ghrelin in obesity is directly related to the decreased smell capacity ⁽³⁵⁾. Gut hormones may alter the perception and pleasantness of specific odors, presumably either directly through their receptors in the olfactory system or indirectly through central interfaces between olfaction regulation systems, appetite control, memory and motivation ⁽³⁵⁾.

Circulating hormones reach the orbitofrontal cortex via cortical-hypothalamic circuits. Concurrently, odor and taste information also arrives to the orbitofrontal cortex via the thalamus and somatosensory cortex. The orbitofrontal cortex integrates this available information and gives a value to the food stimulus ⁽³⁶⁾.

Fatty diets reduce OSN abundance and bulbar projections. There was a reduction in the size of an axonal projection with fat feeding. There should be fewer neurons, because odor enrichment is known to influence OSN survival and production of newborn neurons in the OB ⁽³⁷⁾.

Mature OSNs express the olfactory transduction machinery at the ciliary surface. We anticipated that a diet-induced reduction in OSN abundance should be linked to a reduction in G-protein and G-protein coupled receptor (GPCR) concentration. The effect of diet-induced obesity on the apoptosis and proliferation of the OE determine whether the loss of OSNs was a result of a reduced proliferative activity or an increased death of neurons. High-fat diet may increase the kinetics of regeneration in the olfactory epithelium by increasing the apoptosis of the neuronal population while also increasing mitosis of the progenitor basal cells ⁽³⁸⁾.

Cellular inflammation consequent to a high-fat diet has been described in peripheral tissues, such as liver or adipose tissue, and also within the CNS, including the cortex and hypothalamus. In the hypothalamus, high fat promotes macrophage infiltration and microglia activation, which can lead to the release of proinflammatory interleukins and cytokines, such as IL-1, IL-6, and TNF α that use transgenic models to demonstrate that TNF α can induce apoptotic death of OSN ⁽³⁾.

Chronic exposure to fat in the diet impairs action potential firing frequency and interspike intervals of mitral cells of the OB. Currently, it is demonstrated that there is a reduced EOG amplitude after maintenance on high fat ⁽³⁸⁾. Evidence has also emerged that apoptotic mechanisms and specific proteases can act during development to regulate proper axonal guidance of OSNs ⁽³⁹⁾. An apoptosis regulatory molecule in the OE, causes misrouting of OSN axons to deeper layers of the OB ⁽⁴⁰⁾.

SUMMARY & CONCLUSION

Olfaction is the oldest of the human senses. It allows us to demystify our surroundings, to identify and judge the edibility of foods and to detect impending danger, such as from a predator or fire. It is a critical physiologic process of the nasal airway, mediated primarily by the olfactory nerve. Peripheral and central components of the olfactory

systems, modulate the perception and function of this vital chemical sense.

In conclusion, our study presents strong evidence for a causal relationship between changes in olfactory abilities of obese patients, which demonstrated altered olfactory acuity. Obesity leads to well-supported cardiovascular, inflammatory, and cognitive declines. Consumption of diets high in fat are found to cause nervous system dysfunction. Morbidly obese individuals were found to have lower smell capacity, especially in odor detection and identification. A number of studies have suggested that smell and taste capacity are also modulated by the endocrine system apart from central regulation.

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