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Impact of Metabolic Syndrome on Retronasal Olfaction

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ABSTRACT

As rates of metabolic syndrome (MS) rise globally, it is unclear how and if the risk factors associated with this condition impact flavor perception via the retronasal pathway, which is critical for experiencing the flavor of foods and drinks. This commentary discusses existing literature on the possible impacts of MS on retronasal olfaction by examining primary diagnostic criteria, including hypertension, hyperglycemia, hypertriglyceridemia, hypoalphalipoproteinemia, and excess visceral adipose tissue. Risk factors for MS including hypertension, obesity, and hyperglycemia appear to have a negative impact on the sensitivity of retronasal olfaction. Although most of the work cited in this communication affirms that MS does negatively affect the functionality of the olfactory system, it is important to note that research is divided on this determination. Although retronasal dysfunction is not considered a life threating condition, it drastically changes the landscape of sensory information perceived and impacts an individual's quality of life. Further clinical research on the impact of MS on retronasal olfaction is warranted to provide insights into the intricacies of these pathways.

Keywords

Cardiovascular health, Dietary adaptation, Flavor, Insulin, Nutrition.

Introduction

As rates of MS rise globally without a clear cause, given the diversity of populations impacted [1], a commonly suggested intervention is a lifestyle change, including a heart-healthy diet. Recommendations for a heart-healthy diet include limiting sodium, increasing fruit and vegetable intake, as well as consuming mono- and polyunsaturated fatty acids moderately while reducing saturated fatty acids and refined sugar intake [2,3]. As these dietary modifications deviate from the standard western diet, tailoring recommendations to an individual's taste preferences may improve the success rate of favorable dietary adaptations.

To a greater extent, noteworthy is the impact of the sense of smell, particularly retronasal olfaction, in identifying food flavors and subsequently, creating food preferences [4]. There are two distinct pathways in the olfactory system; olfactory perception refers to an individual's perception of odors via the nasal canal [5]. Retronasal olfaction refers to the perception of odors emanating from the oral cavity during mastication [6].

Conditions impacting taste perception are widely known; ageusia (complete taste losses) and hypogeusia (partial reductions) can result from brain trauma, cancer, nutrition deficiencies, aging, and viral illness such as COVID-19 [7,8]. While these conditions are not always life-threatening, they induce discomfort and can lead to appetite loss and changes in eating habits, with possible adverse health effects.

Research surrounding the impact of metabolic syndrome on the physiological adjustment of an individual's taste preferences is limited. This is particularly the case for flavor perception in the retronasal olfaction pathway. This commentary will discuss the existing literature on the impact of MS on the retronasal olfaction pathway and how it may affect flavor perception.

Metabolic Syndrome and Retronasal Olfaction

For the scope of this commentary, the MS definition proposed by the US National Institute of Health (NIH) was used with primary diagnostic criteria recognized as hypertension (≥ 130/80 mmHg), consistent hyperglycemia (≥ 125 mg/dL while fasting and greater than 180 mg/dL 2 hours postprandial), hypertriglyceridemia (≥ 150 mg/dL), hypoalphalipoproteinemia (< 35 mg/dL), and excess visceral adipose tissue (waistline of ≥ 101.6 cm in males and ≥ 88.9 cm in females) [9]. While a limited number of studies exist that explore the impact of MS on the retronasal pathway, there is a clear consensus that there is a given reciprocation between metabolism and the retronasal pathway.

Hwaung et al. aimed to investigate the relationships of MS and its components with olfactory dysfunction in a representative Korean population. Data were analyzed from the Korean National Health and Nutrition Examination Survey (2008–2010). A total of 11,609 adults who underwent otolaryngological examination were evaluated. Their findings demonstrated that elevated waist circumference, elevated fasting glucose, elevated triglycerides, reduced HDL cholesterol, elevated blood pressure, severe stress, depressed mood, and suicidal ideation were significantly associated with olfactory dysfunction only in women [10].

Research broadly captures the dynamic between metabolic health and retronasal acuity, however the impact of MS on the olfactory system are not conclusive. Gallo et al. observed the prevalence of olfactory dysfunction being higher in American older adults (≥ 40 years of age) with diagnosis of MS, however, after adjusting for co-founders (i.e., smoking and socio-economic status), a significant association of MS and olfaction dysfunction was exclusive to females [11]. Another pilot study by Dicker et al. noted improved metabolic metrics using a novel nasal implantation device to reduce olfactory perception. Participants ≤50 years of age demonstrated reduced olfactory sensitivity, statistically significant weight loss, and self-reported reduced preferences for sweets compared to the control group. As the primary population criteria were age 18–65 years and body mass index (BMI) 30–42 kg/m^2, this study demonstrates the synergy between an individual's present metabolic state, lifestyle change, and acuity of the olfactory system [12]. Orthonasal and retronasal pathways both utilize organs within the olfactory system. The inhibition of chemical routeswith nasal implementation near the olfactory epitelium, these interactions could possibly affect the retronasal acuity altering an individual's flavor perception and ultimately, taste preferences. While this study, as with additional existing literature [13], did not consider MS as such, the cluster of components are discussed in isolation. Overall, MS has proven challenging to capture, one of the reasons being that the phenotypical expression of this condition is not homogenous to the metabolic state [1].

Hypertension and Retronasal Olfaction

Although hypertension is included in all definitions of MS, the impact on the retronasal pathway has not been deeply explored and warrants further investigation. A single longitudinal study exploring the link between retronasal olfaction and hypertension amongst 5000 self-reporting participants found a link between elevated levels of blood pressure and altered taste and smell perception [14]. Similarly, Camato et al., when measuring olfaction acuity, observed that 65% of hypertensive type 2 diabetes participants presented smell identification impairment compared to 18% of non-hypertensive participants [15].

Hyperglycemia and Retronasal Olfaction

Numerous studies have investigated the intricacies between the olfactory system and glycemic state [15,16]. The olfactory system is influenced by energy balance, drives feeding behaviors, and is an essential sensory trigger for the first steps in metabolism. Hormones necessary to metabolic feedback including insulin, leptin and ghrelin have been found in the olfactory bulb and other olfactory processing centers in rodent models [17], demonstrating the importance of the olfactory pathway for metabolic homeostasis. A cross-sectional study indicated a strong negative mediating effect of insulin resistance markers on olfactory sensitivity for food aroma, independent of BMI and hunger state in 75 healthy young participants (with no diagnosis of endocrine or metabolic disorders) of varying weight classifications [18]. Decline in olfactory sensitivity has also been observed in individuals with endocrine disorders including type 1 diabetes and type 2 diabetes [19]. Catamo et al. found that 22% of type 2 diabetes participants had identification impairment in salt taste and 55% with odor recognition compared to control subjects. The authors found individuals with another complication (i.e., hypertension, dyslipidaemia) can worsen olfactory acuity and taste perception [15]. Certain forms of treatments for diabetes can possibly impact the olfactory system, flavor perception, and consequently taste preferences. One study found self-reported hyposmia was observed for type 2 diabetes patients with higher severity of disease using aggressive treatment (oral and insulin treatment) compared to those who reported no use of drug treatment [16]. Although it is clear that glycemic dysfunction impacts olfactory acuity, the relationship of duration of diabetes and the severity of olfactory dysfunction has yet to be investigated [13]. Whether an effect in the opposite direction, from olfactory signals to glycemic regulation, is present and the influence of retronasal olfaction on these pathways, remains unclear and requires further investigation.

Hypertriglyceridemia and Retronasal Olfaction

Although hypertriglyceridemia is an important biomarker for several metabolic disorders such as obesity, diabetes, and cardiovascular disease, limited research has been designated to the impact on retronasal olfaction. Alsayyab and Hirsch observed that patients who had reduced olfaction sensitivity had experienced lipid ageusia demonstrating the integral role of retronasal olfaction for detecting lipids in their study [20]. Alterations in lipid detection capacity could cause distortions in dietary habits and increase dietary fat consumption as sensory feedback pathways are dysfunctional. Additionally, lipid ageusia and taste distortions coincided with an early onset hypercholesterolemia [20]. In contrast, one analysis conducted by Gallo et al. found that among middle-aged men (40–64 years), those with reduced olfaction sensitivity had significantly lower triglycerides compared to normosmic participants [11]. Research is needed to investigate the impact of hypertriglyceridemia on retronasal olfaction and if the link is causation or correlation. Furthermore, study results must be interpreted in the context of variable lipid panels.

Hypoalphalipoproteinemia and Retronasal Olfaction

Alpha-lipoproteins, commonly known as high-density lipoproteins (HDL), are essential for lipid homeostasis and possess antioxidant, anti-inflammatory, and antithrombotic effects. Gallo et al. also found that among middle-aged women (40–64 years), self-reported olfactory dysfunction was associated with higher triglycerides, hypoalphalipoproteinemia, and higher low-density lipoprotein (LDL) with consideration for adjusting for co-founders (ie., smoking and socio-economic class). Measured olfactory dysfunction was not associated with HDL levels but showed significant direct associations with triglycerides and LDL levels, particularly among older adults [11]. Hwaung et al. found that hypoalphalipoproteinemia with other present MS symptoms had negatively impacted olfaction acuity in women as discussed in the metabolic syndrome and retronasal olfaction section above [10]. More research on the impacts of hypoalphalipoproteinemia on retronasal olfaction is needed to define the intricacies of HDL's role in olfaction acuity.

Excess Visceral Adipose Tissue and Retronasal Olfaction

A myriad of research demonstrates the connection between BMI and the olfactory system [21]. An important limitation of BMI is that it does not distinguish between excess fat, type of fat, muscle, bone mass, nor does it provide any indication of the distribution of fat among individuals. Thus, excess visceral fat is a more indicative measure of symptoms to metabolic syndrome [22]. Excess visceral fat is understood to disrupt endocrine pathways as it releases adipokines, influencing local and systematic states of inflammation [23]. Fernandez-Garcia et al. analyzed the relation between fat, fat-free mass, visceral fat, leptin, adiponectin and visfatin and measured olfactory acuity in 179 female participants in various weight classes. They found a negative relation between the olfactory function and those variables related to age and BMI, such as leptin, fat mass, fat-free mass and visceral fat mass ratio (VFR). However, when these variables were corrected in a multiple regression model, the amount of visceral fat was the only variable associated with the decrease in olfactory function [24]. Research evaluating similar parameters is needed in different populations to understand the role of visceral fat in retronasal acuity and the olfaction system.

Suggested Direction for Future Research

As obesity, diabetes, and heart disease rise globally, the impact of MS on retronasal olfaction is difficult to grasp. The MS risk factors of hypertension, hyperglycemia, hypertriglyceridemia, hypoalphalipoproteinemia, and excess visceral adipose tissue overlap within endocrine and cardiovascular specialities, limiting clustering in clinical diagnosis and in research. While there is a plethora of research illustrating the importance of the olfactory system's role in the collecting external sensory stimuli in combination with the internal signals, such as leptin, ghrelin, and insulin to communicate with different brain regions to regulate food intake and energy expenditure [17], the intricacies remain unknown.

Insulin has been found in two major organs of the retronasal pathway: the olfactory epithelium (OE) and the olfactory bulb (OB). The OB has the highest density of insulin receptors and insulin concentration in the central nervous system and it is most enzymatically active against insulin, with the highest rate of degradation [25-28]. Insulin transport through the blood brain barrier into the olfactory bulb has been shown to be two to eight times faster than into the entire brain [25-27]. One possible explanation is the role of inflammation to the disruption of retronasal acuity. As the components of MS increase the risk of inflammation, research indicates it activates and increases the expression of several proteins that suppress insulin-signalling pathways, making the body less responsive to insulin [29]. Insulin resistance in combination with the dysfunction of adipokines released from visceral fat leading to a persistent low inflammatory state is likely to impact the acuity of retronasal olfaction. Jiménez et al. found that diabetic rats displayed impaired olfactory functions which expressed miR-146a, a protein related to inflammation [30]. What remains unclear is the role of flavor in hormonal regulation in olfactory acuity, the inflammation markers related to retronasal deterioration and whether MS-induced inflammation inflicts permanent damage on retronasal acuity.

Although most of the work cited in this communication affirms that MS does negatively impact the functionality of the olfactory system, it is important to note that research is divided on this determination. Poessel et al. concluded that insulin resistance did have a negative correlation with olfactory function, a similar finding in our narrative. However, they found no effect of obesity status, BMI, metabolic factors, or body fat percentage on neural responses to food odors. An important distinction was that participants were noted to be metabolically healthy as they were screened and discriminated against history of an endocrine disease diagnosis. In their discussion, they addressed that the processing of food odors in the brain may be different in obese individuals who have other risk factors (i.e., hypertension, hyperglycemia) when compared to healthy obese counterparts [31]. This asserts the need for research to investigate how metabolic dysfunction, including but not limited to MS, impacts olfaction acuity in weight diverse populations. Another question prompted is at what degree of inflammation is retronasal acuity impacted and what biomarkers are available to investigate this.

Most work cited investigates the olfactory system either by evaluating both orthonasal and retronasal olfaction or either orthonasal or retronasal olfaction in isolation. However, there is very little research determining specificity of retronasal acuity as results were obtained from self-reported surveys. As data collection has less barriers with survey collection, the distinction between taste perception (mediated by taste buds) and retronasal acuity is difficult to distinguish. Research on MS risk factors with methods specific to retronasal exclusively are needed to define parameters of significance on flavor perception and metabolic homeostasis.

Although retronasal dysfunction is not considered a life threating condition, it drastically changes the landscape of sensory information perceived. Studies indicate that metabolic syndrome changes taste preferences [32] towards more calorically dense food items. Although research has begun to reveal MS impact on retronasal olfaction, investigation of each MS component is paramount for further clarity. Ultimately, through the understanding of MS on the retronasal system, it will be possible to develop sustainable nutrition interventions.

Conflicts of Interest

Manuscript authors are employed at air up GmbH.

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