



# The Most Updated Diagnostic Tests in Olfactory Assessment; a Review

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## ABSTRACT

**Background:** People are usually faced with rhinological disorders such as Hyposmia and Anosmia. There are currently subjective and objective tests to evaluate olfactory sense. Subjective and screening tests as well as measuring olfactory sense threshold have been commonly used to assess Hyposmia and Anosmia. Identification and discrimination tests have been qualitative methods to assess olfactory sense. Objective methods have been predominantly used in research field; sometimes, they are used for lawful cases as the following: Single Photon Emission Computed Tomography (SPECT), Functional Positron Emission Tomography (FPET), Functional Magnetic Resonance Imaging (fMRI), and olfactory stimulated potential. **Materials and methods:** In the current study, the articles of databases such as Springer, PubMed, and Google published from 1990 to 2017 were studied. The key words were evaluating olfactory sense, olfactory test, Anosmia, and screening olfactory tests. **Discussion:** Measuring and evaluating olfactory sense helped in understanding a comprehensive spectrum of nasal disorders' impacts. This issue is important particularly before rhinological surgeries, since disregarding olfactory disorder in the patients might lead to increased medical complains and accusing physicians of the surgeries which caused olfactory dysfunction. There are currently various olfactory screening tests, which could be used to evaluate the olfactory sense function.

**Key Words:** olfaction disorders, olfaction, identification tests, discrimination tests.

eJPPR 2020; 10(4):120-125

**HOW TO CITE THIS ARTICLE:** Mohammad Aghajanjpour, Alireza Mohebbi (2020). "The most updated Diagnostic Tests in Olfactory Assessment; a review", International Journal of Pharmaceutical and Phytopharmacological Research, 10(4), pp.120-125.

## INTRODUCTION

Although olfactory sense is one of the main quintuplet senses, its importance has been ever underappreciated in comparison with optic and auditory senses. There are many questions relating to anatomy and physiology of olfactory sense which has remained un-responded. Low intention of the scientists to do more research in this field could be one of the reasons. It is obvious that olfactory sense is of substantial importance in diagnosing dangerous materials such as spoiled foods, contaminants, and toxic gases. Studies have indicated that olfactory potency is based on individuals' genetic feature [1]. The human being is able to diagnose more than 10 thousand smells [2].

It has been estimated that human olfactory spectrum ranges from 100 to 400 mm<sup>2</sup> [3]. Human olfactory neuro-

epithelium is located in posterior plane of nasal dorsum, superior turbinate, and upper part of nasal septum [4].

The olfactory disorder could be both transient or permanent. The disorder is usually presented in a tract transferring particles to olfactory neuro-epithelium; while in the permanent disorder, the inadequacy is indicated in olfactory receptors, and the dysfunction is also presented in Central Nervous System (CNS) relating to olfactory sense. Concussion, sinonasal diseases, contacting with toxic chemicals, smoking, and endocrine disorders (e.g., hypothyroidism, mellitus diabetes, Kallmann syndrome, nephro-hepatic dysfunction) could be demonstrated as the reasons of olfactory sense dysfunction [5]. Extensive literature has indicated that aging is accompanied by olfactory loss and Hyposmia and/or Anosmia which is also a feature of several neurodegenerative disorders [6].

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**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest .

**Received:** 17 SDecember2019; **Revised:** 02 July 2020; **Accepted:** 08 July 2020



The previous studies reported the prevalence of olfactory sense as being 1% to 3%, whereas some studies reported this amount as being 15.3% [7]. In investigating ENT outpatients without the history of sinonasal diseases and/or head and neck malignancies, the incidence of Hyposmia and Anosmia was reported to be 16% and 5%; respectively [8].

Various aspects of olfactory sense could be evaluated including olfactory sense threshold, and identification and discrimination tests of olfactory sense. Identification test of olfactory sense has been the most common method to assess the olfactory sense dysfunction. The aforementioned test could be used to screen the olfactory dysfunction in general population [9].

Nowadays, the clinical importance of olfactory identification was emphasized in diagnosing some neurodegenerative diseases (e.g., Parkinson disease) [10]. The olfactory sense could be evaluated in three perspectives as the following:

- Olfactory sense perception in rare concentrations (olfactory threshold)
- Non-verbal diagnose of various smells (olfaction discrimination)
- Ability in expressing objects' smells (smell identification)

The olfactory sense could be used to discriminate more than thousand smells; thus, the total investigation of this sensorial system could not be carried out with some simple tests. Particular tests could be used to evaluate some aspects of olfactory sense based on the data obtained. Quantitative evaluation of olfactory sense is important in rhinology, since Hyposmia and Anosmia resulted from olfactory conducting disorder is a common sign of allergic rhinitis or chronic rhino-sinusitis, and also a disease such as early multiple sclerosis [11, 12].

Measuring qualitative disorders of olfactory sense which is called Dysosmia (Kakosmia or Parosmia) is difficult; notwithstanding, the specific tests have been proposed to evaluate the qualitative disorders of olfactory sense. In total, the olfactory tests have been categorized as subjective and objective tests [13].

## METHOD AND SOURCES:

In the current study, the articles of databases such as Springer, PubMed, and Google published from 1990 to 2017 were studied. The key words were olfactory sense evaluation, olfactory sense, olfactory test, Anosmia, and screening olfactory tests.

### The Clinical Tests to Evaluate Olfactory Sense:

Gustatory and olfactory senses: Although gustatory and olfactory senses are independent of each other, differentiating their disorder should be based on taking the

history into account, which is difficult. Patients with olfactory or gustatory disorders often complain of Ageusia at the preliminary stage. For instance, the patient might report that they could not percept sauce taste after head trauma, as a matter of fact, his/her olfactory sense was changed. The absolute disorder of gustatory sense is too rare; therefore, a simple test could be used to assess gustatory sense before applying any procedure to evaluate the olfactory sense. The liquids with salty, sweet, sour, and bitter tastes could be used to evaluate the gustatory sense [14].

### Subjective Tests:

The subjective tests have been commonly used to assess the olfactory sense, since the pace is executable. The individual tests were assigned to 3 classes as the following:

- Screening
- Quantitative
- Qualitative

### The Screening Tests to Evaluate the Olfactory Sense:

These tests should be prompt, validated, and inexpensive. A usual case of this test was collecting bottles of coffee, chocolate, perfume, etc., and then investigating nose orifices separately. Some of the screening tests included University of Pennsylvania Smell Identification Test (UPSIT), Odor Stick Identification Test (OSIT), Scandinavian Odor Identification Test (SOIT), and Sniffin Sticks test [15]. The UPSIT was used in North America in 1984. The UPSIT was a multi-optional test; there were 4 options for each odorant. The patient must have selected an option even he/she does not feel any smell. This test took 10 to 15 minutes, and contained 40 odorants packed in crystals. Each odorant was located on a brown films crushed with a pen. The Anosmia, Hyposmia, Parosmia, and even simulation could be diagnosed with UPSIT [16]. The two prompter versions of UPSIT were introduced to screen the olfactory disorders including Cross Cultural Smell Identification Test (CC-SIT) and Pocket Smell Test (PST). CC-SIT was a duodecimal test of odorants, which could be undertaken less than 5 minutes of course with a confidence coefficient lower than UPSIT; therefore, CC-SIT might be able to differentiate normal smell of an un-normal one, but except for diagnosing simulation. In PST, 3 odorants were prepared for the patient, if he/she could not diagnose one or more odorants' smell, UPSIT would be performed for him/her. According to the study of Duff et al., PST with high accuracy could be used to differentiate patients with Alzheimer of healthy subjects [17].

San Diego Test was another identification tool. This test was inexpensive and easily performed. In San Diego Test, 6 common odorants including kid powder, chocolate, cinnamon, mustard, almond oil, and coffee packed in opaque bottles were prepared for the patient, he/she would

be asked to smell one of the odorants and select a picture of 20 in the tray; in this test, speaking disorder would not be a hinder for performing the test [18].

Sniffin Sticks Test is another screening test that took 4 minutes long, approximately; in this test twelve odorants with the concentration more than threshold were provided for the patient. Similar to UPSIT, it was a multi-optional test; finally, the correct answers would be collected, and the ultimate finding would be regulated based on age, and gender of the patient [19].

In Smell Diskette Test (SDT), 8 polyester diskette containing odorants were provided for the patient; there was an odorant (i.e., vinegar) stimulating trigeminal nerve to diagnose simulation. This test was undertaken in less than 5 minutes [20].

Barcelona Smell Test - 24 (BAST-24) was another screening test; in this test, 20 and 4 odorants stimulating olfactory and trigeminal nerves were used; respectively, and then the patients were asked to answer 4-optional questions. This test took 20 minutes long, approximately. Studies reported BAST-24 as a worthwhile clinical test [21]. In a study performed by Gerami et al., 16-material test was used consisting of 15 and 1 material(s) stimulating olfactory and trigeminal nerves; respectively. Using vix in lieu of ammoniac to stimulate trigeminal nerve in their study had more prominence than the other tests, since ammoniac has a sour and unfavorable smell and could damage to olfactory system [22]. Biolf smell test was another method to diagnose the olfaction's potency and threshold with the help of 8 and 3 various odorants in different concentrations; respectively [23]. Sniff Magnitude Test (SMT) was also a test to evaluate the olfactory sense function by measuring the smell decrease level facing to rancid materials. Rancid and odorant materials are differently processed in the brain [24].

Frank et al. reported that SMT was not affected by memory, attention, and cultural backgrounds, since maintaining or verbal response was not needed in this part [25]. Bensafi et al. indicated that the unfavorable smells were prompter processed and assessed than the favorable smells; they also reported that the right hemisphere of brain was predominant in processing unfavorable smells [26].

#### **Quantitative Tests to Evaluate Olfaction:**

Quantitative tests evaluate the olfaction threshold in various odorants. Quantitative tests need more time, and are beneficial to monitor Hyposmia grade, although they are not able to discover the cause of the olfaction disorder, and present diagnoses or preliminary therapeutic information. Nowadays, there are many tests available to evaluate the olfaction threshold using n-Butanol as a stimulating material. In these tests, the least concentration of n-Butanol diagnosed by each individual was assessed. Connecticut Centre Chemosensory Clinical Research

(CCCCR) threshold test and European Test of Olfactory Capabilities (ETOC) were the quantitative tests used for measuring the olfaction function and efficacy. Anosmia could be differentiated from normal olfaction by CCCCCR and ETOC. In addition, CCCCCR and ETOC could be used for evaluating Hyposmia. Using olfactometer is another accurate method to measure the olfaction threshold. The aforementioned tools were used for presenting accurate concentrations of odorants. These methods as being time-consuming, complicating, and expensive, are usually used in particular centers [27].

#### **Qualitative Tests to Evaluate Olfaction:**

Evaluating and measuring Dysosmia is difficult. The patients with Dysosmia supposed their expression of olfactory sense would change with difficulty. Nevertheless, specific tests were designed to evaluate some of the olfaction disorders. Identification and discriminations tests were used for evaluating the potency of special smells and the ability of the patients to differentiate various smells; respectively. Sniffin Sticks Extended Test Battery (SSETB) was a test evaluating the olfaction qualitatively and quantitatively [28].

#### **Objective Tests to Evaluate Olfaction:**

Olfaction dysfunction has been clinically categorized as of central and peripheral types. Trauma, respiratory upper tracts infection, and smoking have been the most common causes of Anosmia [29]. The traumatic reasons of olfaction dysfunction included tension damage of neurons' axons in olfaction area, brain pulse, and hemorrhage in areas relating to olfaction perception and change in sinonasal tract. These factors have often been treated both medically or surgically. The olfaction function was improved in 10% of the cases, however its improvement was not perfect [30]. The regeneration of the damaged neurons might improve olfaction after traumatic injury. Animal studies showed that the disrupted axon of olfactory nerve might grow along the cribriform plate, and communicate with bulbus olfactorius [31]. The respiratory system upper tract infection has been the most common reason of infectious Anosmia. Although patients with Anosmia showed no sign of disorder in radiographs following the infections, the virus could damage the olfactory epithelium [32]. Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) could portray CNS pathology details together with measuring bulbus olfactorius, and also other anatomic structures in central olfactory system of the patients with Hyposmia and healthy subjects; nonetheless, these modalities could not provide information about the olfaction function [33].

Objective evaluation of olfaction was difficult, and depended on investigating CNS following the olfactory stimulators. The malingered patients could be diagnosed by this method. Using olfaction stimulation potential is a

usual objective method. Functional Magnetic Resonance Imaging (fMRI) and Functional Positron Emission Tomography (FPET) have been the modern techniques to evaluate olfaction. CNS changes following olfactory nerve stimulation could be demonstrated by fMRI and FPET. These techniques have been currently used in research field, but they could be used in clinical settings [34]. Eftekhari et al. reported Single Photon Emission Computed Tomography (SPECT) as an alternative for fMRI in diagnostic evaluation of the patients with post-traumatic olfaction impairment. The more accuracy of SPECT than fMRI was indicated in the current study findings [35]. Gerami et al. expressed SPECT as a beneficial technique in evaluating cerebral post-traumatic Anosmia. As compared to the study of Eftekhari et al., the severity and type of olfaction disorder was determined in the study of Gerami et al. [36]. Levy et al. found that cerebrum performance in 9 cerebral areas of patients with Anosmia to the 3 olfaction stimulating materials including pyridine, menthol, and amyl acetate was lower than the healthy subjects; this finding was more apparent in inferior plane of frontal and cingulate lobes as well as medial and posterior planes of temporal cortex [37]. In a study of investigating cerebral activity in response to olfaction stimulation in patients with congenital Hyposmia using fMRI, the cerebral activity of the patients was reported; however, this activity was lower than the healthy subjects and the patients with acquired Hyposmia. Furthermore, there was a close correlation between post-traumatic olfaction impairment with cerebral perfusion using SPECT [38]. In the study of Furtak et al. on determining the cerebral blood flow changes after mild head trauma, SPECT was demonstrated as a more accurate tool than CT scan, SPECT was also able to illustrate cerebral perfusion disorders and EEG changes simultaneously [39]. SPECT could be used to investigate post-trauma cerebral perfusion in forensic pathology [40]. In the study of Nardo et al. on patients with post-trauma Anosmia, using SPECT, it was indicated that patients with Anosmia apparently had low perfusion than the healthy subjects in all the olfactory areas. Their study showed that SPECT could be used as a qualitative objective tool in evaluating neuro-pathophysiology and forensic pathology issues relating to olfaction [41].

## DISCUSSION AND CONCLUSION

Based on the previous studies, 1% to 2% of the Americans aged lower than 65 years of age suffered from olfaction disorder, and more than 200 thousand people referred to the physician with the complaint of the olfaction impairment annually. These statistics illustrated the importance of olfaction assessment using related tests. The olfaction disorder has been a common issue in rhinological

patients [42]. Evaluating the olfactory sense would help to understand a comprehensive spectrum of nasal disorders impacts. This issue is important particularly before rhinological surgeries, since disregarding olfactory disorder in the patients might lead to the increased medical complains and accusing physician to a surgery caused olfactory dysfunction. In a study done before on nasal surgery, the olfaction impairment was observed in 10.3% of the patients, hereupon, using common tests to assess the olfactory sense before sinonasal surgery would be an enterprise in preventing the accusation of the surgeons [43].

Moreover, the olfactory tests could be used for comparing the treatment effects after sinonasal surgery. Although objective tests have been currently used in the research field, it is expected to use them in clinical settings in the near future. Evaluating the pre- and post-operative olfaction is a main enterprise to reduce the damage to the olfactory mucosa, since olfactory impairment would reflect the underlying disease etiology [44].

The authors declared that there was no conflict of interest.

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