World Journal of Otorhinolaryngology-Head and Neck Surgery (2015) 1, 28—33

Available online at www.sciencedirect.com

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journal homepage: www.keaipublishing.com/WJOHNS; www.wjent.org

REVIEW ARTICLE

Olfactory dysfunction and its measurement in the clinic

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Received 20 September 2015; accepted 22 September 2015
Available online 26 October 2015

KEYWORDS
Allergy;
Polyposis;
Nasal disease;
Rhinosinusitis;
Smell;
Psychophysics;
Olfaction;
Iatrogenesis

Abstract The sense of smell is largely taken for granted by laypersons and medical professionals alike. Indeed, its role in determining the flavor of foods and beverages, as well as in warning of, or protecting against, environmental hazards, often goes unrecognized. This is exemplified, in part, by the fact that most patients presenting to medical clinics with "taste" problems are typically subjected to complex brain imaging and gastroenterological tests without the sense of smell even being tested or considered as a basis of the problem. Aside from frank deficiencies in sweet, sour, bitter, salty and savory (umami) sensations, "taste" disorders most commonly reflect inadequate stimulation of the olfactory receptors via the retronasal route; i.e., from volatiles passing to the receptors from the oral cavity through the nasal pharynx. This article describes the two most common procedures for measuring the sense of smell in the clinic and provides examples of the application of these tests to diseases and other disorders frequently associated with smell loss. Basic issues related to olfactory testing and evaluation are addressed. It is pointed out that smell loss, particularly in later life, can be a harbinger for not only a range of neurodegenerative diseases, but can be a prognostic indicator of early mortality.

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Peer review under responsibility of Chinese Medical Association.

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http://dx.doi.org/10.1016/j.wjorl.2015.09.007

Introduction

Smell loss or distortion is a common problem encountered by the otolaryngologist. Such dysfunction is often reflected in complaints of "taste" loss, with many patients noting that food "tastes like cardboard" or no longer has hedonic appeal. Diminished smell sensitivity influences food selection and nutrient intake, and compromises safety from food poisoning and toxic agents. Indeed, a disproportionate number of the elderly die in fires, gas explosions, and toxic exposures as a result of being unable to detect smoke or odorous warning agents added to natural gas.[1] Smell dysfunction can be devastating for those who depend upon this sense for their safety or livelihood, such as cooks, homemakers, plumbers, fire fighters, perfumers, fragrance sales persons, wine merchants, food and beverage distributors, and employees of numerous chemical, gas, and public works industries. Indeed, according to medical regulations, anosmics are not allowed into the U.S. armed forces, reflecting the importance of smell function in the operation of complex machinery and the potential for exposures to toxic agents in the battlefield.

As is the case with vision and hearing, quantitative testing is essential to (a) determine the validity and nature of a patient's complaint, (b) accurately monitor changes in function over time (including influences of pharmacological, surgical, or immunological interventions), (c) detect malingering, and (d) establish disability compensation. Fortunately, largely as a result of funding from the U.S. National Institutes of Health in the early 1980's, significant advances have been made in the development and application of easy-to-use and reliable clinical tests of olfactory function — advances described in this paper. It is clearly is no longer tenable to simply ask a patient whether a few odorants placed under the nose can be identified, since this approach can result in misleading conclusions, as it is not quantifiable, lacks reliability, has no normative referent, and is easily faked by malingerers.

Basic considerations in measuring smell function

The sense of smell is sensitive to thousands, if not millions, of odorants. While accurate testing of such a sense appears, at first glance, to be daunting, smell function is relatively easy to measure. Thus, with some exceptions, when psychophysical thresholds are increased to one odorant they tend to be increased to others, reflecting the commonality and distribution of the receptor cells and their propensity for injury.[2] Analogous phenomena are present for the identification of different odorants. Injury to more central neural structures similarly influences pathways that code or transmit information from more than one class of receptor cell. For these reasons, responses to only a few well-chosen target odorants need to be evaluated to establish an accurate assessment of the overall functioning of the system. The reader is referred elsewhere for detailed information on the anatomy and physiology of the olfactory system.[3]

In recent years, both psychophysical and electrophysiological tests have been developed to quantify olfactory function in the clinical setting. Additionally, modern structural and functional imaging procedures have been applied to better define the underpinnings of functional losses, such as damage to or the lack of olfactory bulbs and tracts.[4] However, olfactory tests vary in terms of sensitivity and practicality, ranging from brief tests of odor identification to sophisticated olfactometers yoked to electrophysiological recording equipment capable of quantifying odor-induced changes in electrical activity at the level of the olfactory epithelium (the electro-olfactogram; EOG) and cortex (odor event-related potentials; OERPs). Psychophysical tests are more practical and less costly than electrophysiological tests, making them much more popular, particularly in light of technical issues with electrophysiological testing. For example, the EOG cannot be reliably measured in all patients, given epithelial sampling issues and the intolerance of some subjects to electrodes that are placed within their non-anesthetized noses. Since the EOG is present in some anosmics and can be recorded even after death, it cannot be used, by itself, as a reliable indicator of general olfactory function. Unlike the auditory brainstem evoked potential, the OERP is presently incapable of localizing anomalies within the olfactory pathways. OERP recording sessions can be quite long since relatively long inter-stimulus intervals are needed to prevent adaptation.[5]

Some physicians, as well as attorneys seeking to denigrate psychophysical test results, divide sensory tests into "subjective" and "objective" classes. The former require a conscious response on the part of the examinee, whereas the latter assess involuntary reactions, such as altered electrical or autonomic nervous system activity. However, as pointed out for audition by the Nobel laureate Georg von Bekesy nearly 50 years ago, such a dichotomy is misleading and laden with a value judgment, since objective always trumps subjective.[6] In fact, most psychophysical olfactory tests provide a more sensitive assessment of function than do electrophysiological measures. While it is presumed that "subjective" tests are easier to malinger than "objective" tests, forced-choice psychophysical tests can detect most malingerers on the basis of improbable responses,[7] and many so-called "objective" olfactory tests are not immune to malingering. For example, reliable measurement of electrophysiological responses requires considerable subject cooperation, such as sitting very still during recording sessions.

Modern psychophysical olfactory tests

The utility of a clinical olfactory test depends upon its reliability (consistency, stability), validity (accuracy in measuring dysfunction), and practicality (administration time and effort). Related to its validity are its sensitivity (ability to detect abnormalities), specificity (ability to detect abnormalities with a minimum of false positives), and positive predictive value (the proportion of all positive tests that are true positives). Unfortunately, too few data are available to allow for statistically valid comparative assessment of such parameters among the dozens of olfactory tests that are presently available,[2] although, in general, the more trials contained in a test, the higher its