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Review Article

A brief history of olfaction and olfactometry

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Abstract

The sense of smell has been a cause for speculation and fascination over the centuries. An appreciation of odours has been deeply rooted in many cultures, including ancient civilisations such as the Egyptians. The level of understanding of the anatomy and physiology of olfaction which our ancestors had was slight, and much remains to be discovered. This paper explores the progression of knowledge over the years to the present day. Particular emphasis is placed on odour classification and olfactometry, and on the techniques whereby great scientific minds have sought to quantify that human sense which is arguably least quantifiable. A review of some of the current methods of olfactometry is included within this remit.

Key words: Smell; Special Senses Disorders; History

Introduction

Olfaction is phylogenetically the oldest sense, and humanity's interest in scents or odours can be traced back into ancient history. The ability to smell is often taken for granted, and we often overlook the enjoyment of many daily pleasures it enables, such as the smell of good food or perfume. Our forebears held this sense in high regard, yet their understanding of the anatomy and physiology of olfaction was slight. Still today, olfaction remains the least well understood of our senses. Odours have enjoyed a very prominent cultural significance from the point of view of health and disease over the centuries. Stench or miasma was synonymous with disease, and in the nineteenth century perfume workers were said to have lower rates of cholera and tuberculosis infection. Various scholars have, over the centuries, contributed towards our understanding of olfaction, and some of the ways in which they sought to measure olfactory ability are described below.

> That which we call a rose, By any other word would smell as sweet. (Shakespeare, 1597)[1]

Odour classification

One of the factors central to the understanding of the complexities of olfactory perception has been the classification of odours into a small number of large groups. John Amoore is often credited with the classification of primary odours in 1952;[2,3] however, this task was actually achieved nearly 200 years earlier. Carolus Linnaeus (1707–1778) is famous for his system of classification of plants and animals, and yet it is almost unknown that he suggested a seven-category system for odours, as follows: camphoraceous, musky, floral, pepperminty, ethereal, pungent and putrid.[4–6]

However, Linnaeus was clearly frustrated by a lack of understanding of the underlying physiological mechanisms of olfaction, as evidenced by his 1752 quote from his own book *Odores Medicamentorum*:

> If we better understood the theory of the nervous function then we would understand the basics of smelling much easier. Until now we are not sure if the functioning of our nerves happens with a free liquid which is flowing from end to the other or whether that there are vibrations that cause the nerves to function. It is not sure if stimulation is the only cause of nerve function.[7]

A hundred years later, Hendrik Zwaardemaker (1857–1930), a Dutch physiologist, revised Linnaeus's system and proposed nine olfactory categories: ethereal, aromatic, fragrant, ambrosiac, alliaceous, empyreumatic, hircine, foul and nauseous.[8]

In 1916, Hans Henning (Figure 1) felt that a 'smell prism' using six primary odours would better represent the range upon which human olfaction was based. He theorised that any olfactory stimulus would occupy a position in this three-dimensional space, as follows: flowery, foul, fruity, spicy, burnt and resinous.[6,9]

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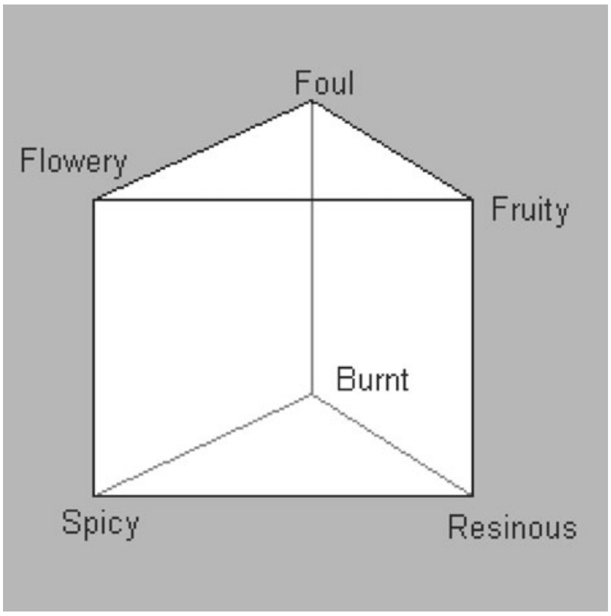

FIG. 1
Henning's smell prism.

In 1927, Crocker and Henderson devised a system involving four basic odours: fragrant, acid, burnt and caprylic (i.e. smelling like a goat). This system became a commercially available product comprising a kit with comparison vials, each labelled with the basic odour and its position on a nine-point scale (odours were rated from zero to eight).

The current lack of any universally agreed and standardised odour classification system underlines the fact that this is still a contentious area.

Olfaction and thinking

The influence of the hedonic properties of odours on thinking, creativity and memory has been in the minds of scientists for many centuries. Voltaire (François-Marie Arouet, 1694–1778) and René Descartes (1596–1650) separately believed there was a link between olfaction and emotion. Jean-Baptiste Rousseau (1671–1741) was believed to have stated:

> To learn how to think we need to exercise our organs and senses . . . . The smelling sensation is the sense of the imagination; it touches the nerves so must stimulate the brain more intensely.[10]

Unpleasant smells were also a source of inspiration to many, including Elizabeth I, who wore the smell of rotten apples, cinnamon and clove on a necklace.

Gabriel Garcia Marquez (born 1927) needed yellow roses to concentrate on reading. Wilhelm Busch (1832–1908) also used the smell of flowers for inspiration: 'Hier auf dem Dreifuß unterm Flieder Sitzt er bereits und dichtet wieder', which translates as 'Here he is sitting under the lilac Making poems again'.[10]

In the mid-nineteenth century, Eugene Rimmel (1820–1887) invented the 'perfume-fountain', the first specimen of which was presented at the World Exhibition of London in 1851.[10] Based on distilled water vapour, he also developed a 'room-perfumer', the 'Rimmel Vaporiser and Aromatic Perfume Disinfector', which proved its outstanding effect in overcrowded and poorly ventilated public rooms. In addition to suitable conditioning of the air, the process was supposed to positively influence thought and mood amongst the occupants.

The hypothesis that olfaction has a significant influence in the process of human thought has been strengthened by the observations of German researchers. At the beginning of the twentieth century, a schools inspector in Brandenburg reported that the different smells of plants and flowers, as well as chemical smells, had different effects on school pupils, having a positive effect on their learning capacity.[11] More recently, Susanne Kerl conducted olfactory experiments on schoolchildren aged nine to 11 years using the odours jasmine, lavender, rosewood and sage.[12] The children were categorised into three groups according to their anxiety level and were then asked to rate the hedonistic properties of these odours. Amongst many descriptors, more than half of the children in the first two anxiety level groups preferred rosewood to fall asleep.

The advent of olfactometry

In the nineteenth century, efforts to assess olfaction were solidified by Gabriel Valentin (1810–1883) in 1842 and Passy in 1892. Valentin was the author of several important works addressing, amongst other topics, the blood and its circulation, muscle and nerve impulse conduction, digestion, toxicology, and the physiology of the senses.[13] From 1836 to 1843, he published the *Repertorium für Anatomie und Physiologie* ('Repertory for Anatomy & Physiology') and collaborated on many professional journals.[14,15] Passy's work involved investigating the quality of odorants in conjunction with their molecular structure.[16] However, it was Hendrik Zwaardemaker (Figure 2) who, at the end of the nineteenth century, was the expert in olfactory experimentation. 'We live in a world of odour' he remarked in *L'Année Psychologique*.[17] Zwaardemaker developed a device for measuring olfactory thresholds. This consisted of a short pipe constructed from odourless kaolin, which was placed in the nasal cavity, and scent-carrying capsules held within a metal cylinder. The smell intensity was varied by altering the angle of the pipe.

Olfactory testing in the twentieth century

To date, the largest study of olfactory disturbances has been undertaken by the National Geographic Society in 1987; 1.5 million people in the USA were tested with the odours mercaptan, eugenol, isomyl-acetate (banana), galaxolid and androstenone.[18]

During the twentieth century, the greatest development in olfactory testing took place in the last

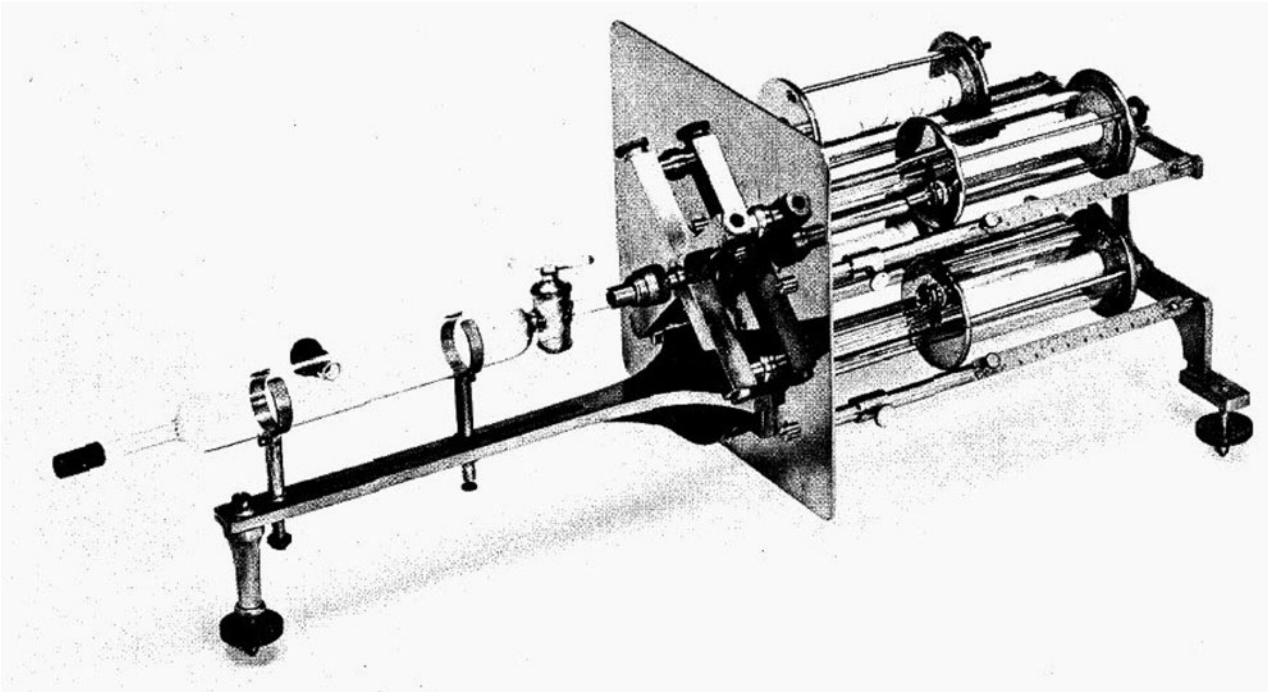

FIG. 2
Zwaardemaker olfactometer, The Netherlands, 1886.

20 years. Various tests were devised, including a number of standardised and practical psychophysical tests. The University of Pennsylvania Smell Identification Test, devised by Richard Doty *et al.,*[19–21] (Figure 3) remains the 'gold standard' in qualitative assessment. Prior to this, the Connecticut Chemosensory Clinical Research Center Test was a forerunner in the USA.[22]

FIG. 3
University of Pennsylvania Smell Identification Test kits.

The University of Pennsylvania Smell Identification Test is a 40-item test which employs microencapsulated ('scratch and sniff') odorants. It is available in English and three European language versions and can be self-administered in 10 to 15 minutes, with only a non-medical member of staff required to mark the results. The test provides a percentile rank of a patient's performance relative to age- and sex-matched controls, as well as categorising the patient into one of the following groups: normosmia, mild microsmia, moderate microsmia, severe microsmia, anosmia or probable malingering.

The Smell and Taste Center at Philadelphia (Figure 4), under the leadership of Richard Doty, has been at the forefront of olfactory assessment

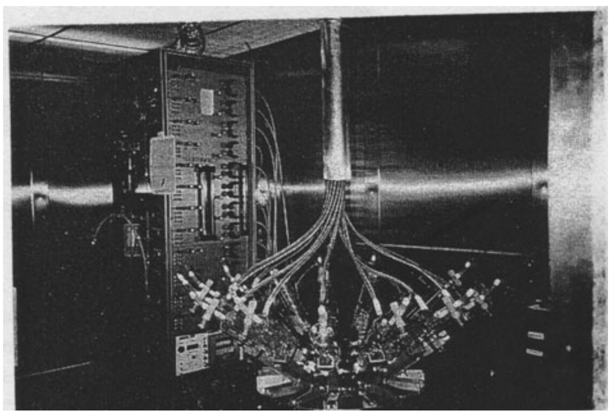

FIG. 4
Dynamic air-dilution olfactometer, University of Pennsylvania.

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for the last 20 years. Despite the monopoly of the University of Pennsylvania Smell Identification Test in the USA, this test cannot be used without adaptation in Europe due to cultural differences regarding familiar odours. Doty and his colleagues attempted to counter this by developing the Cross-Cultural Smell Identification Test.[23] However, these tests collectively are expensive, costing US$27 per individual booklet, and they have not proved universally popular within European healthcare systems.[24]

Olfaction in Europe

In the European arena, the Dresden Smell and Taste Clinic has stamped its own mark on developments in the field; its answer to the University of Pennsylvania Smell Identification Test is the 'Sniffin' Sticks' (Figure 5) test.[25–27] This is a more comprehensive test devised by Thomas Hummel and his colleagues in Dresden, who have an equal calibre of experience in researching olfactory disorders. The Sniffin' Sticks set costs about £400, but, if utilised regularly, probably represents a more cost-effective than the aforementioned test kit, with refills available for the pens that comprise the odour sticks. The Sniffin' Sticks set combines odour identification with odour threshold testing and odour discrimination. This means, of course, that the concept of self-administration is lost due to its greater complexity, although a recent study in Vienna suggested that self-directed testing with the identification component only yielded equally valid results.[28]

Other European tests have been launched over the last few years, and include the European Test of Olfactory Capabilities,[29] the Barcelona Smell Test-24[30] and the Combined Olfactory Test.[31] The European Test of Olfactory Capabilities seeks to provide a pan-European assessment of olfaction and uses a combination of a supra-threshold test and an identification task, which has been tested and retested on populations in France, Sweden and the Netherlands. Despite some weaknesses with the ETOC study, it appears to have good test-retest reliability. In the UK, the 'Combined Olfactory Test has been validated in a combined study with a New Zealand population.[31] This test comprises a simple threshold test using 1-butanol, in conjunction with an identification test using 10 odours. The test has a very similar format to the Connecticut Chemosensory Clinical Research Center Test and is a little crude, but it has the advantages of being quick and easy to perform, as well as very affordable in the UK National Health Service setting as underlined by a more recent study.[32]

FIG. 5
'Sniffin' Sticks' test kit.

Current developments in olfactory testing

Threshold measurement is a quantitative evaluation of olfaction and theoretically the most precise. However, qualitative testing with identification test formats continues to be the most popular type of olfactory test in use. In this respect, Japanese researchers have also been active in developing olfactory tests to suit their cultural setting, most recently through the development of 'Odour Sticks', their answer to Sniffin' Sticks.[33] This test encompasses danger odours, such as gas, rotting and burning, as well as culturally specific odours, including Japanese orange, Japanese cypress, natto and Indian ink. The test uses a forced choice format, but, rather than smelling the sticks directly, the sticks have a creamy core which is applied to paper and then presented to the subject.

Whilst the assessment of olfactory perception pattern and the measurement of olfactory threshold for a specific odorant have been previously considered,[34] these parameters are not widely accepted, and variations between different centres are seen for common odorants such as phenethyl alcohol.[35–39] In addition, the effect of certain variables on olfactory perception trends has been considered,[36] and models of olfactory disturbance have been proposed.[40]

The measurement of olfactory event-related potentials uses an olfactometer to deliver olfactory stimuli to a subject wearing electroencephalogram electrodes, in order to detect specific cerebral activity related to olfaction.[41,42] The magnitude and timing of olfactory event-related potentials give information about the processing of signals from the nose to the olfactory cortex, and are dose-related responses. Such results are free from cognitive influences and a qualitative response can be seen, with different odours stimulating different areas of the olfactory cortex. It has been possible to localise centres, by topographical comparison of the amplitudes of olfactory event-related potentials, and to derive an olfactory 'map' of the brain. However, this technique is an expensive resource and is only available in a few specialised centres. Although the technique is able to demonstrate differences between normal and abnormal subjects, it is at present unable to detect specific defects in the olfactory pathway, the major advantage of OERPs is that if positive, anosmia can be excluded.

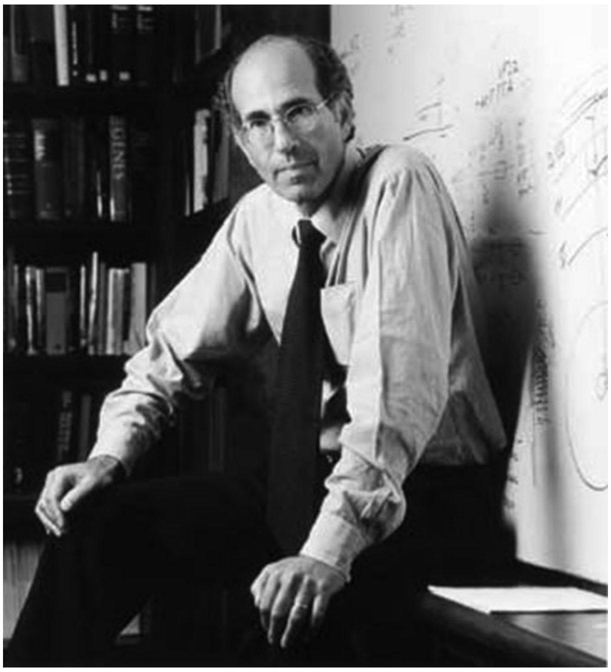

FIG. 6
Richard Axel.

Olfaction and olfactometry: the future

Most recently, Linda Buck and Richard Axel (Figures 6, 7), who became Nobel Laureates in physiology in 2004, achieved the greatest breakthrough in the understanding of olfaction to date. They discovered a large gene family, comprising some 1000 different genes (three per cent of the human genome) which gives rise to an equivalent number of olfactory receptor types. Each olfactory receptor cell possesses only one type of odorant receptor, and each receptor can detect a limited number of odorant substances. This means that each receptor cell is therefore highly specialised for a few odours.[43] This important piece of the olfaction jigsaw will surely be the first of many more, enabling a greater understanding of this sensory modality.

FIG. 7
Linda Buck.

In the late twentieth century, the debate continued over accessory olfactory pathways, such as the vomeronasal organ.[44,45] Such pathways have clearer roles in other members of the animal kingdom, as demonstrated by recent research,[46,47] and remain at present an unknown factor in human olfaction. The field of olfaction and its testing certainly remains a developing realm, with pioneers such as Richard Doty and Thomas Hummel leading the way. The artificial or electronic nose is a recent development which may find a useful role in qualitative assessment in areas such as the food industry; however, it is at present by no means able to mimic the human olfactory apparatus or to achieve quantitative assessment.

The creation of a smell map for odours akin to visual fields or auditory thresholds across a frequency range, is one 'holy grail' for otolaryngologists and scientists interested in olfaction. Others may include better therapeutic modalities for olfactory disorders. Some early progress has already been achieved by the likes of Dawes *et al.*[48,49] The only certainty in olfaction research is that a greater understanding and a more robust test format must surely lie in the future.

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