Future perspectives in smell and taste disorders

J.-S. Lacroix* and B. N. Landis**

*Departments of Otolaryngology Head and Neck Surgery, University of Geneva Medical School and Geneva University Hospitals, Geneva, Switzerland; **Department of Otolaryngology Head and Neck Surgery, University of Dresden Medical School, Dresden, Germany

Key-words. Olfaction; taste; medical treatment; anosmia

Abstract. Future perspectives in smell and taste disorders. Large sections of the medical community have, in the past, thought of human olfaction as a minor sense that was destined to disappear soon. This view has changed completely in the last two decades. This article will attempt to highlight the most important recent advances in our understanding of the human olfactory function and focus in particular on questions for the future and developments required in this field.

Introduction

Smell and taste disorders have been underestimated by the medical community for some time.1 By contrast with the view in the past that this was a lower sense, evidence is now emerging that human olfaction and taste are far more effective than previously believed.2 This article is an attempt to highlight the most important recent findings in chemosensory research and it raises the most urgent unanswered clinical questions.

Achievements

A comprehensive overview of chemosensory achievements over the past two decades is difficult since olfaction and taste represent two distinct modalities that have been thoroughly investigated in different species. We will therefore concentrate exclusively on clinical and human findings. This article follows the structure of an outpatient consultation, starting with the elements recently identified in the patient history and then proceeding to diagnosis and treatment.

a) Patient history

A proper and careful patient interview can yield diagnostic hints in almost 70 to 75% of all cases of smell and taste disorder.3 The most prevalent causes of olfactory disorders, like head trauma, sinonasal problems or postviral olfactory impairments, can be ascertained simply through questioning. The patient history is therefore a key element in the routine workup of chemosensory disorders.4 Consequently, enquiries should be made about the onset, duration and possible accompanying sinonasal or general symptoms. Recent reports also stress the fact that certain elements like parosmia and phantosmia are rarely spontaneously reported by the patients,5 but that they are a source of valuable diagnostic information because they are more likely to occur after postviral or posttraumatic injury to olfaction.6 Similarly, questions should regularly be asked about neurodegenerative symptoms and the presence of similar diseases in relatives since olfactory disorders might be an initial symptom of a disease.7 Although little systematic knowledge is available, enquiries should be made about medication, and about professional and environmental exposure to known olfactory toxic substances.8

b) Examination

Huge improvements have been achieved within the last 30 years in the standardisation and normalisation of olfactory and gustatory testing. Good and cheap tools are now easily available9-11 and every investigation of chemosensory disorders should be completed by testing smell and taste. Simple questioning has repeatedly been shown not to reflect the measurable chemosensory function.12,13 Measurements of this kind can also ascertain chemosensory improvement, even though the perceived amelioration is moderate, and therefore help to monitor olfactory function very reliably over time.14 The debate about whether lateralised testing should be performed routinely remains

B-ENT, 2009, 5, Suppl. 13, 133-136
unresolved. Endoscopic examination is mandatory since the prevalence of asymptomatic nasal polyposis is relatively high in the general population. By contrast with taste, the objective assessment of olfactory function has been available in the routine clinical setting for almost a decade with olfactory evoked potentials. Unfortunately, this technique remains time-consuming and olfactometers are expensive and fragile in maintenance. However, almost all western European countries now have ENT centres housing expertise about this kind of objective olfactometry.

c) Diagnosis

As mentioned above, the diagnosis of olfactory impairments is mainly based on patient history. Nevertheless, in about one quarter of cases, no clear origin can be found for the olfactory disorder. In these cases, thorough diagnostic workup is warranted and, over the last twenty years, there have been new insights into the possible reasons for smell disorders. Firstly, a large body of research has found that most neurodegenerative disease is accompanied by impaired olfactory function at a very early stage of the disease. Discussions are ongoing about the extent to which olfaction may serve as a biomarker. Secondly, imaging of the olfactory system has been improved to a point where MRI can now not only be used to exclude a brain tumour, but also to quantify the olfactory bulb volume and correlate this volume to olfactory function. Finally, a recent report showed that patients with lupus erythematosus suffer from decreased olfactory function. This suggests that autoimmune and inflammatory diseases favour olfactory disorders, and future investigations will have to show whether this is also the case for other diseases.

d) Treatment

Smell

Although our knowledge about olfactory disorders has improved considerably, the treatment options are still quite limited. Apart from the treatment of olfactory impairment due to sinusosal disease, no curative treatments have yet been medically proven for other causes. However, the last five years have clearly shown that the spontaneous recovery rates for post-viral and post-traumatic olfactory disorders are far better than previously reported. This is valuable information and should be given to the patient. Furthermore, the prognostic value of olfactory distortions like parosmia and phantosmia has been clarified. In contrast to what might be intuitively thought, they predict neither better nor poorer recovery. Despite the limited treatment options, there have been several trials. Some of them have claimed promising results for medical treatment with, for example, alphalipoic acid, caroverine, local citrate buffer and xanthine derivatives, while others find no effect for vitamins or zinc. A very interesting recent study suggested that smell training could improve olfactory function.

Taste

In general, it can be stated that the frequency, causes and treatments have been less well studied in the case of taste dysfunction than in the case of olfaction. Psychophysical taste testing has just become standardised and treatment options have scarcely been studied. Nevertheless, we feel that we should mention promising studies of the effect of zinc on taste dysfunction. Although the mechanism is totally unclear, this medication seems to help a considerable number of subjects and trials will not be harmful because zinc has no side-effects.

Open questions

a) Patient history

When it comes to obtaining more information from the patient, the focus in the future must be on elements that may identify still-unknown origins of olfactory disorders. These elements may include environmental exposure, medication and drug intake, as well as the accompanying symptoms. The past has shown that patients with olfactory disorders do not necessarily mention all the important elements and tend to link their olfactory disorders to factors which might not be the real cause.

b) Examination

Although current testing methods are standardised, they still cover an insignificant range of the olfactory system. Compared to vision and hearing, where the audible frequencies and visible wave lengths are limited, it is yet not known how many million odours can be smelled. Even the best clinical tests examine only the capacity to recognise up to 50 odours, which is a fraction of the possible number. Furthermore, all humans have specific anosmias and possible odours which all of us smell. The question of which
odour receptors remain functional in all humans because they are important for recognising odours that are meaningful to humans remains unexplored.\textsuperscript{41} We must also not forget that there is still no objective or even psychophysical test to assess qualitative olfactory disorders (e.g. parosmia, phantosmia). A more systematic evaluation of these olfactory distortions could generate new insights into pathophysiological processes in olfactory impairments.

c) Diagnosis

In all outpatient clinics and even with the best workup, up to 20 percent of all patients receive a diagnosis of idiopathic olfactory impairment. Further work must focus on the fields that have not yet been adequately explored. Do blood markers improve the diagnostic process? Does olfactory bulb morphology allow for the diagnosis of neurodegenerative diseases or prognoses? Since the olfactory epithelium is easily accessible and harvesting olfactory neurons is feasible, this could be a valuable source of information about olfactory impairment. However, although promising attempts were published ten years ago, the analysis of olfactory biopsies and histology is not yet part of the routine workup in olfactory outpatient clinics.\textsuperscript{42} Further efforts must be made to integrate olfactory tissue specimens in the diagnostic process. As mentioned above, olfactory tests could serve as biomarkers for certain neurodegenerative diseases. However, the tests currently available are not specific enough on their own to diagnose diseases like Parkinson or Alzheimer’s.

d) Treatment

Most of the studies mentioned here are flawed in that they are not placebo-controlled. This makes it difficult to distinguish between olfactory improvement due to medication and improvements that occur naturally in spontaneous recovery. In addition to medical treatment, further efforts could also be made in the area of engineering for olfactory stem cells prior to re-implantation.\textsuperscript{43} Surgical treatment options for olfactory impairments could also be investigated further. With the exception of case reports, surgery in the olfactory cleft still remains a rarity which deserves more attention.\textsuperscript{44}

Final Remarks

To conclude this outlook, we wish to emphasise that our understanding of human olfaction must be seen within the context of a sense which has always been considered to be minor. Consequently, olfactory research has not attracted the same attention as vision and hearing research. In this light, it is particularly encouraging that the Nobel prize for physiology was awarded to researchers who have significantly revived research into olfaction in the past twenty years.\textsuperscript{45} Although many questions about olfaction remain open, the field has become very active and fruitful research in this previously underestimated branch of ENT is emerging almost every month.

Acknowledgements

This work was supported by a grant from the Swiss National Fund for Scientific Research (SSMBS grant n° PASMA-119579/1) to BNL.

References

12. Landis BN, Hummel T, Hugentobler M, Giger R, Lacroix JS.


J.-S. Lacroix and B. N. Landis

Jean-Silvan Lacroix
Rhino- Olfactology Unit
Department of Otolaryngology
Head and Neck Surgery
University of Geneva Medical School and University Hospitals
Rue Michelli-du-Crest 24
CH-1211 Geneva Switzerland
Tel.: +41/22/382 82 62
Fax: +41/22/372 82 40
E-mail: Silvain.Lacroix@hcuge.ch