PHYSIOLOGY AND PATHOPHYSIOLOGY OF OLFACTION

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Up till now, olfaction has been the sense organ which has been the most neglected. There are however many reasons to expect that in a short time this will change very decisively. In recent years physiologists have done a lot of work on this subject and have made great progress.
We can divide the problem of olfaction into different parts in order to make the subject clearer. For this reason we will try to answer the following questions: 1. What are the recent theories about olfaction i.e. what is the modern vision on the way in which the odorivectors influence the olfactory mucosa; 2. Along which pathways does the neural activity reach the brain; 3. In which fields of the brain do the impulses of olfaction arrive, and 4., last but not least, the main subject of this article: what can be said about the pathophysiology of the sense of smell.

Ad 1. What are the modern theories. It would be better to say what **is** the modern hypothesis about the olfaction. In order to reach the olfactory mucosa, the odor has to penetrate the most livious passages of the nose, on the walls of which many of the molecules are absorbed. During normal respiration only 2% of the molecules may strike the olfactory epithelium. Thus in order to smell we will have to sniff just as dogs do. The olfactory cells have filaments or cilia, probably about one to twenty or perhaps far more per cell. In this manner the receptory surface of the olfactory mucosa is enormous, probably exceeding the receptory surface of the entire human body.
Obviously smell is a matter of surface. But what happens on this surface? It was **Amoore** and his co-workers who in 1963 launched a very attractive theory about it. Before these investigations it was already known there were seven groups of odors: ethereal, camphoraceous, musky, floral, minty, pungent and putrid ones. What are the characteristic differences between these seven groups? It turned out that each of the first five groups (i.e. the ethereal, camphoraceous, musky, floral and minty group) have molecules which show great similarities in weight and in shape. The pungent group is a group of small molecules, which has a negative charge and the putrid group consists of small molecules with a positive charge. This was the reason why **Amoore** drafted his stereochemical theory of odor. It is the **shape,** i.e. the stereochemical properties, which determine the odor of a substance (fig. 1). The surface of the mucous membrane has holes and the odorivectors fit into these holes as a key into a key-hole. It was **Dravnieks,** who gave a further dimension to this theory with his physical-chemical basis of olfaction. He proposed the following model:

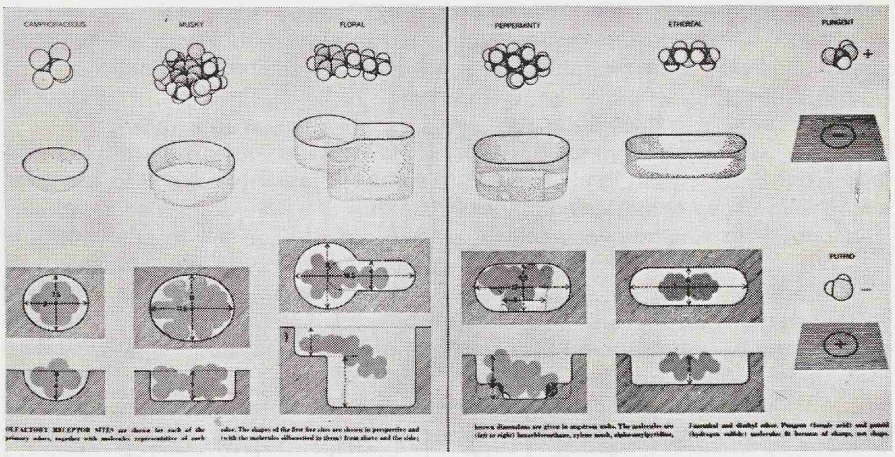

Figure 1. Stereochemical theory of olfaction (from: Amoore John E. c.s., Scientific American feb. 1964).

The charge donor and accepter molecules are larger and at their junction they form cavities of specific shapes and sizes, which serve as the absorption sites for the odorivector molecules — the 5 or 7 odorivector groups of **Amoore** (fig. 2).

Ad. 2. The pathways of the impulses through the neural tissues. The olfactory mucosa has about 50 millions of olfactory cells. Every cell has, as is said, one to twenty, perhaps far more, cilia. These cilia come from a little

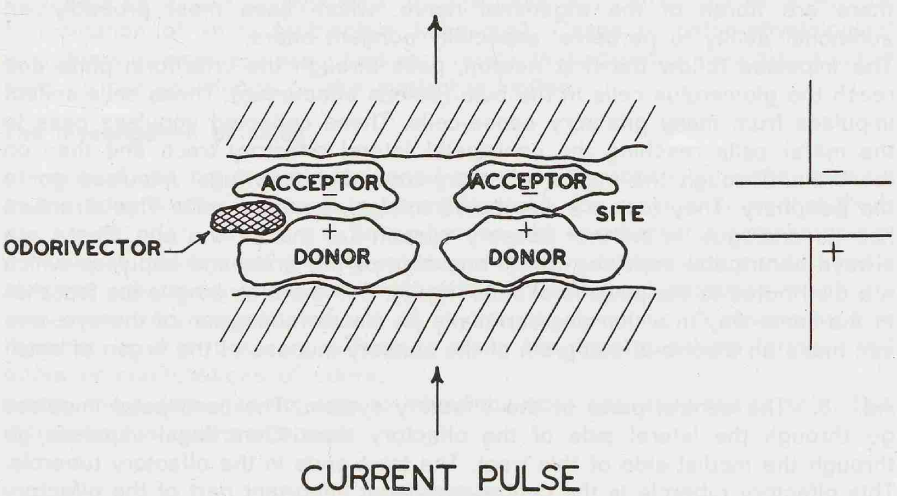

Figure 2. Model of olfactory chemosensor, proposed by A. Dravnieks (from Dravnieks, A., 1964, Physicochemical basis of olfaction, Annals of the N.Y. Academy of Sciences 116, 2, 429).

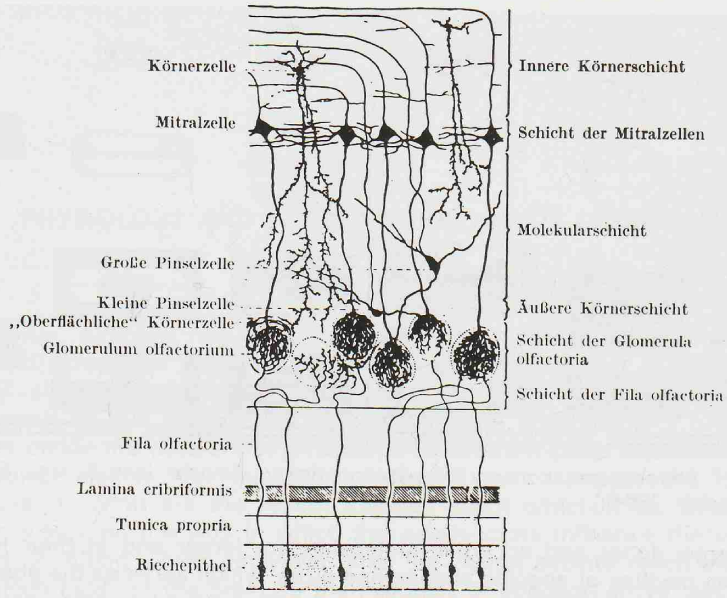

Figure 3. Structure of the mucosa and the olfactory bulb (from: Bargmann, W. (1956): Histologie und micr. Anatomie des Menschen, 665, G. Thieme, Stuttgart).

bulb, found at the end of the long cell. In the middle of the cell the nucleus is situated and from here the neuron begins. The neurons form bundles — the fila olfactoria which go through the cribriform plate. Beside this system there are fibres of the trigeminal nerve, which have most probably an additional ability to perceive, especially pungent odors.
The impulses follow the first neuron, pass through the cribriform plate and reach the glomerulus cells in the bulb (bulbus olfactorius). These cells collect impulses from many olfactory sense-cells. These collected impulses pass to the mitral cells reaching the centripetal lateral olfactory tract, and then on the brain. Through the medial olfactory tract the centrifugal impulses go to the periphery. They too, are distributed to many sensory cells. This structure has its analogue in another sensory system i.e. that of the eye. There are always centripetal impulses which one sent to the brain and impulses which are distributed to the peripheral cells (fig. 3). Still more striking is the fact that in the same way in which one can make an electroretinogram of the eye, one can make an electro-olfactogram of the sensory mucosa of the organ of smell

Ad. 3. The central parts of the olfactory system. The centri**petal** impulses go through the lateral side of the olfactory tract. Centri**fugal** impulses go through the medial side of this tract. The tract ends in the olfactory tubercle. This olfactory tubercle is the central and most important part of the olfactory system of the brain.
From here the fibers go mainly to the anterior pyriform cortex and to the temporal pyriform cortex, both situated in the rhinogenic sulcus. This part

of the cortex forms the cortical projection of smell. Of course there are many parts of the brain that have a second-line connection with the rhinogenic area, e.g. the hypocampus. So far for the physiology and the neurophysiology of smell.

Ad. 4. But now our main subject: **the pathophysiology.** The abnormal functions of this system are: 1. anosmia, 2. dysosmia or par-osmia, 3. kakosmia. This latter can be objective or subjective. The most common cause of anosmia is a blockade of the upper nasal part by swelling: hyperplasia of the mucosa. The reason is so obvious that we will not discuss it further.
Infection, specially influenza, gives destruction of the neural epithelium. A remarkable fact, however, is that the sensory epithelium has the possibility to regenerate. It has been proved in animal experiments that in many cases this regeneration will take place in about six to twelve months. In man too, anosmia caused by influenza can heal in some months.
As you will know there is a special tumor of this region, the esthesio-neuroblastoma. This kind of tumor makes out about 3% of all tumors of the nose. In some cases there is an anosmia, in other cases there is a parosmia, but in many cases the smell is not hampered. A fracture through the cribriform plate can cause an anosmia. In some of these cases there will be a liquorrhoea through the nose too. A high pressure of the cerebrospinal fluid, e.g. by a tumor in the frontal lobe, can also give anosmia by pressure on the bulb. Lesions in many places in the temporal lobe can give parosmia. That lesions in the mucosa or in the bulb may give parosmia, is understandable for it is probable that special flavours are percepted in special regions in the mucosa and in the bulb.
There are two kinds of kakosmia. The fetor can be produced e.g. by a chronic sinusitis and the patient himself smells this (objective kakosmia). The kakosmia may also be a sort of dysosmia. In this case you can speak of a sort of hallucination of smell (subjective kakosmia). Cases of patho-physiological alterations of smell are described very rarely. In diagnostics they play a minor part. So our knowledge on this subject is limited.

The investigation of smell

For clinical use, only the old-fashioned odor-box is practical. Only the contents of the odor bottles will have to be modernised, for we now know that there are 7 basic odors. We have to fill the bottles with an ethereal, a camphoraceus, a musky, a flowery and a minty substance and two bottles with a putrid and a pungent substance. The olfactometers for physiological purposes which are sometimes very complicated are of no use for the clinic. A reason for this rejection is, that it is very difficult to clean the apparatus from former used odors or combinations of odors.
Finally the patient has not only to inhale the odor but really has to sniff. This increases his odor-perception.

RÉSUMÉ

La physiologie de l'olfaction est jusqu'aujourd'hui un sujet bien négligé par les médicins. Neanmoins il y a des progrès très prometteurs dans ce domaine.

L'hypothèse stereochimique de l'olfaction (Amoore, Dravnieks e.a.) est la seule qui peut expliquer les très bas seuils du sens olfactif. Les études stereochimiques ont prouvé qu'il y a sept odeurs de base: l'odeur de menthe, de fleurs d'essence, de camphre, de musc et les odeurs acides et putrides. L'auteur donne un exposé de la structure histologique et fonctionelle de l'organe olfactif.

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