بسم الله الرحمن الرحيم

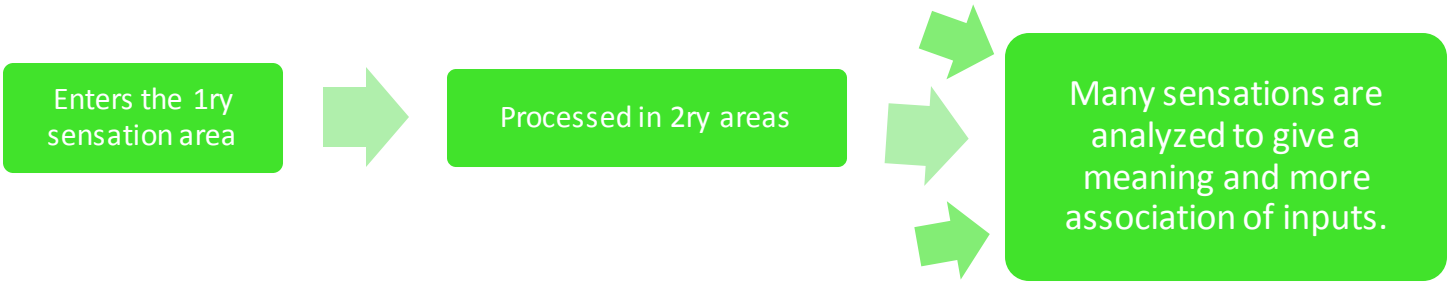
THE CHEMICAL SENSES:

OLFACTION AND GUSTATION

SENSATION IN THE CORTEX

When sensations eventually reach the cortex, they are processed. Thereof, the cortex was divided by the physiological function into primary, secondary and association cortex. The primary cortex in sensation is the first area that receives the sensation (*from* thalamus) and in the motor is the one that directly communicates with the motor. When the sensation arrives, it enters through the thalamus into the primary cortical area where it is detected, and then analyzed for a meaning.

- So first any sensation enters the primary area then gets processed in the secondary areas, after that all this information must be integrated to give a complex meaning, thoughts and higher functions in the association cortex which has areas that have more than one modality of sensation which usually form the higher functions.
- In brief, the following diagram illustrates the route of sensations going to the brain:



GENERAL TERMS: APRAXIA AND AGNOSIA

- Apraxia is the inability to perform complex movements although there is no paralysis in any muscle.

In apraxia, the premotor and the supplementary were damaged/defected which correspond to secondary motor cortex. Premotor is called premotor because the secondary areas in motor do the processing first then the movement occurs unlike in the case of sensation where the sensation first arrives then it gets processed. So after a damage to the secondary motor cortex, the person still can move but they cannot 'make' a meaning for that move (there is no complex movement to perform a designated task).

Same principle applies to the sensation: If the 'tract' of the sensation or the primary area was damaged, there will be a loss of sensation. But if the secondary areas of sensation were damaged, there will not be a meaning for that sensation. This is termed ***agnosia***. For example, if the olfactory area was damaged -> olfactory agnosia. Visual area -> visual agnosia. Auditory area -> auditory agnosia. Sometimes a submodality of a certain area can be damaged as in the case of damaging the part that recognizes trees in the visual area -> tree agnosia (shape). Color -> color agnosia and so on. *So agnosia is a general term that literally means 'I cannot recognize or interpret that sensation in that particular meaning.* The defect can be either in the secondary or association areas.

THE OLFACTORY SYSTEM

Olfaction is the ability to smell. The olfactory system starts in the nasal cavity, the nasal epithelium in the nasal cavity or olfactory epithelium. The olfactory epithelium is constituted of three main cell types, which are:

1. *Receptors*: olfactory receptor neurons, almost bipolar type of cells. The first pole has *cilia* with receptors on them and the other sends sensory fibers. Their function is to detect the chemical signals and transfer it into electrical signals.
   - The neurons cannot live by themselves so they need support and this is the function of the next type.
2. *Supporting* cells: the columnar epithelial cells which provides mechanical, chemical, environmental and food support to the neurons.
   - Those are exposed to the external environment therefore the neurons die and renew themselves in a continuous process every one to three months; this is the function of the next cell type.
3. *Basal cells*: which are undifferentiated cells that are responsible for the regeneration of both the neuronal and supporting cells.

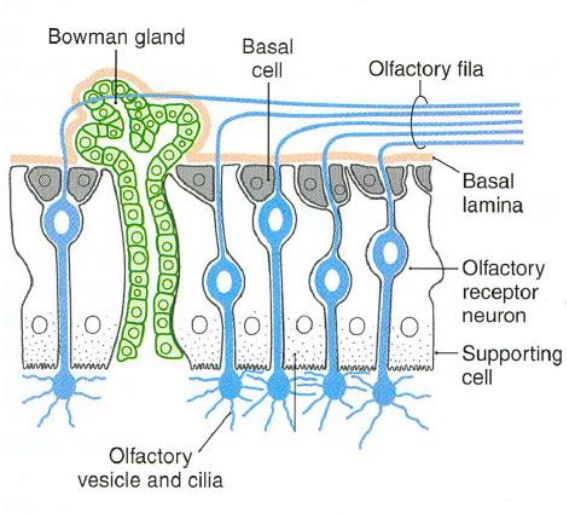


Figure 1: The olfactory epithelium

THE PROCESS OF OLFACTION

It is a chemical sensation wherein chemicals should bind to receptors so the chemicals must be dissolved in a media, and this is the function of the Bowman cells/glands; first it secretes fluid to dissolve the chemical substances then some mucus for lubrication and protection of microbial infections or whatever.

Next, the receptors in the neurons will send the axons centrally and enter the skull through the *cribriform* plate (which is in the roof of the nasal cavity and has many pores through which the axons could pass) and there on the plate they will synapse with the second-order neurons in the *olfactory bulb*. The olfactory bulb is the enlargement at the ending of the olfactory nerve and tract. Also in the synapse, there is come processing in that enlargement.

The connection between the first-order neurons (i.e. the receptors) and the second-order neurons (i.e. the olfactory bulb neurons) does not happen as one-to-one connection, rather, in a magnificent gathering/collection known as ***glomeruli*** or a glomerulus as single. In the glomeruli, there is convergence and divergence where three or four receptors will gather at one neuron (convergence) or a single neuron sending to more than one neuron (divergence). All those help in processing of olfaction even at the level of the olfactory bulb.

Note that all receptors of chemical sensation work through 2nd-messenger type of receptors. One of the most important characteristics of the 2nd-messenger signal is that it gives complex response not only opening or closing of a channel but also affecting proteins, structures and the most important being the *signal amplification*. It is way more potent because it amplifies the signal, which allows detection of lower thresholds of sensations since it is going to be amplified.

Humans smell thousands of odors. However, it is impossible to have thousands of classes of receptors. There could be one hundred classes of receptors and the reason of smelling thousands is *because of the glomeruli, its distribution and the mixing.* So mixing will allow identification of more odors. Also notice that in many of the special sensations and mainly in the olfaction and vision, there are cells whose function is to extend themselves horizontally between the glomeruli and the connections and this helps more and more in processing. (Horizontal red cells in **figure 2**)

The last function in the olfactory bulb is *adaptation*. **Consider this**: if you enter a flower shop for example, you first smell strong scents then after two minutes you no longer smell anything, this is adaptation. There are many levels of adaptation; on the receptor itself, it binds a chemical substance -> gets activated -> the cell then blocks it by adding or removing cAMP or internalization et cetera…

Now **consider this**: you sprayed some perfume in the morning, you smelled it for a minute then it is gone. Then you met someone who admired your perfume and so you started to smell it again. What is the explanation?

- A: Olfactory adaption occurs at the level of receptors, this is one part. But the other part and the main adaption which helps in processing and adaption together is some fibers coming from the olfactory cortex to the olfactory bulb and there it will induce either inhibition or stimulation of the glomeruli at the second-order neurons. Inhibition when there is adaption and *stimulation in case of processing*. This is the function of the centrifugal fibers shown in **Figure 2**.

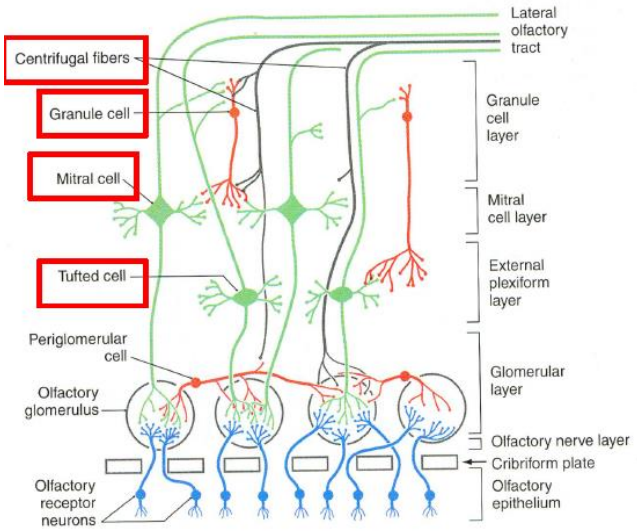


Figure 2: Notice the following: 1) The red horizontal cells which help in more mixing and processing. 2) The centrifugal fibers which help in processing and adaptation.

- So in the end, we can differentiate between smells because of the presence of many subclasses of receptors and different combinations in the glomeruli which make different transduction mechanisms reaching the second-order neurons in red and green as in **Figure 2** where processing, inhibition and centrifugation occur.

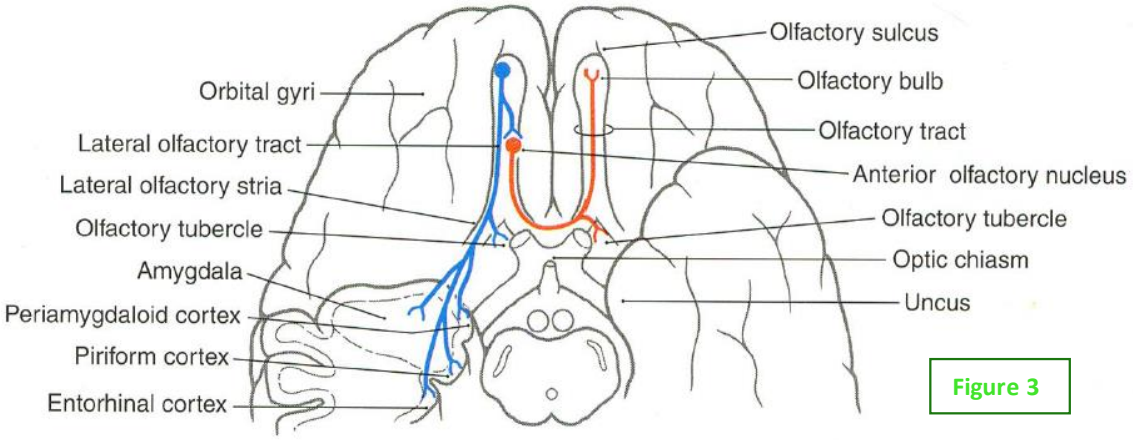


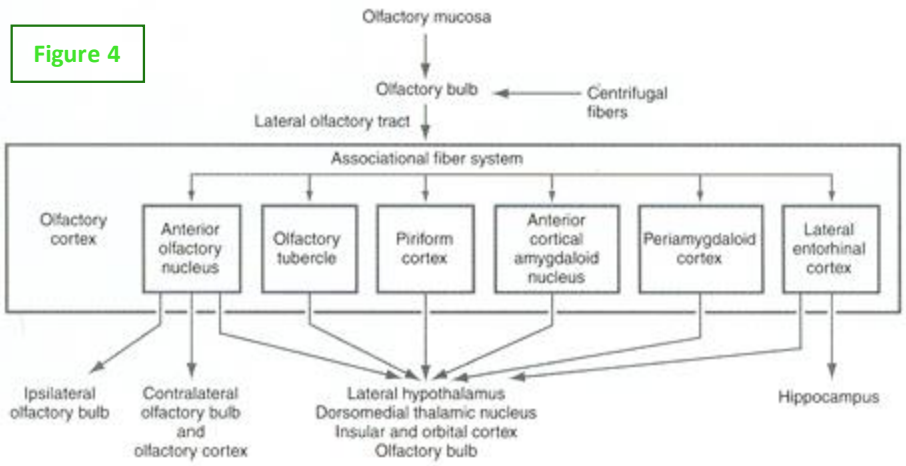
Figure 3

- (Continuing with the sensation route, **figure 3**) After that, from the olfactory bulb, the sensation goes to the olfactory tract to the central areas where it divides into two pathways: the 1) *medial part* usually synapses in the middle of the tract over something called the anterior olfactory nucleus, its function is to *make the processing at the olfactory bulb* and do the crossing and connection between the two sites (at the level of the olfactory bulb and the bulb-cortex). Most of its fibers' target is either to the *second* olfactory bulb or ipsilateral olfactory bulb and a few to the cortex. 2) The *lateral part/tract* keeps going from the olfactory bulb directly to the central areas.

In the ALS pathway, there was 'something' that goes to the cortex, through thalamus to the cortex to provide perception of the ALS modalities. There was also another 'something' that stops at the brainstem then to the hypothalamus and to other numerous places.

Accordingly, the one that will enter the cortex will follow the rule of neocortex-through-thalamus while the other does not target the neocortex - sometimes the target is the paleocortex as in the limbic system which should not pass through the thalamus-. The same principle applies here, *two thirds* of the lateral tract and the olfactory system will pass through the thalamus and from the thalamus to the neocortical areas and this is very important for giving meaning and processing of olfaction. While *the other third* will go to the other areas that are associated with reflexes of olfaction (smelling food makes you hungry), internal regulation, emotion, feeding, hunger, hypothalamus, anger, emotions like amygdaloid and some old cortices that are associated with primitive processes and functioning (paleocortex). The old cortices are olfactory tubercle, piriform cortex, anterior amygdaloid, periamygdaloid and entorhinal cortex, this is the first third. While the other two thirds will go to the dorsomedial thalamus then to the olfactory cortex that is nearly in the same area on the medial and inferior part of the temporal lobes, (**figure 4**.)

Figure 4



Now, for more processing, the sensation will go to the secondary cortex and from there to the multimodal cortex that is the association cortex. One of the most important areas of secondary cortices (also has a slight relation with the association cortex) is the orbitofrontal cortex. From there it provides the meaning of the olfactory sensation especially the right side (which is more important than the left side.) So if the right side is gone, the person can smell but cannot know what exactly they smell. Reflexes may get affected.

If the tract was damaged, there will be a loss of sensation and this called anosmia or hyposmia whether complete or partial loss. The most common cause is that the chemicals did not bind to the receptors and this happens in case of edema, inflammation of the nasal cavity, cold or flu, sinusitis… A cut in the tract can occur due to a trauma, mostly a trauma to the face, the first and the most famous part to be broken is the cribriform plate that will cut the first order neurons axons -> anosmia. In the case of a little cut or no inflammation, basal cells will regenerate and the axon will reach its destination again (temporary loss of sensation). But in case of inflammation, inflammation damages the 'guidance queue' so no correction can take place -> forever loss.

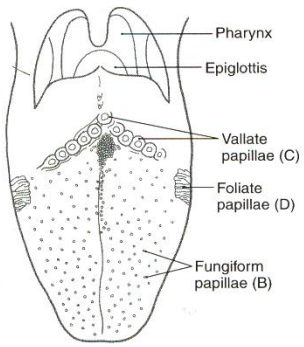
Other degenerative diseases like Huntington's or Alzheimer's have continuous loss of sensation especially the olfactory. You are required to read them from the following references:

- *Disorders of the Olfactory System (page 704-707),*
- *Disorders of the Gustatory System (page 716)*

THE GUSTATORY SYSTEM

Gustation is the sense of taste. The gustatory system in brief is: 'chemical substances tasted at the tongue'. There are taste receptors gathered as taste buds that will send to the second-order neurons. The taste buds are arranged in anatomical and histological complexes not haphazardly, the complexes are called papillae ((s.)papilla), they are distributed almost equally over the tongue and from there the taste sensation starts, (**figure 5**.)

Figure 5: taste buds



There are five modalities of taste: 1) **Salty**. 2) **Sweet**. 3) **Sour**. 4) **Bitter**. 5) **Umami**: (tastes meat or amino acids); monosodium glutamate is a main stimulator for that bud and it is one of the food enhancers. Each of them will activate different type of receptors/different way through channels or blocking or 2nd messenger (not important.)

The gustatory pathway starts from the receptor buds and travels through the nerves (there are three main nerves; the 7th, 9th and 10th cranial nerves, arranged from the anterior of the tongue to its posterior to the oral cavity) that will eventually transfer the sensation to the brainstem where they will synapse at the solitary tract and nucleus (**figure 6**) and from there they will ascend to the thalamus passing through *the central tegmental tract* then synapsing in the *ventroposteromedial* part of the thalamus and from there the third-order neurons will reach the cortex, *the main primary cortex is in the inferior part of the postcentral gyrus*. This sensation, in contrast to other sensations, is almost exclusively ipsilateral.

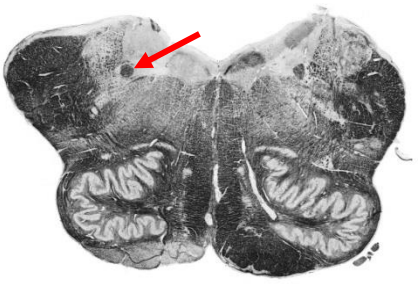


Figure 6: location of the solitary nucleus

If the taste was lost, this is called *aguesia* or hypoguesia whether complete or partial loss. Again, the most common cause is the inability of the chemical to bind to the receptor but there are other cases that are usually neglectable (like hairy tongue, enlargement of the upper surface of the tongue and the presence of deposits due to smoking), however it is mainly due to *the lack of saliva*. No matter how thick the tongue or how big the groove, it all depends whether there is a good solvent or not. So any condition that reduces the saliva would affect gustation, the main cause for this is chemotherapy and radiotherapy for cancer treatment. Medications that cause dry mouth could also do lead to hypoguesia or aguesia. And there is progressive loss of taste in diabetic patients. Also, the loss might be due to damage in the tract before reaching the cortex, usually due to vascular lesion in the medulla or the brainstem.

Q: Now since there are only five modalities of taste how can we recognize a lot of flavors?

A: By smelling; that is why food loses its flavor when you have a cold. Actually, the food will activate the olfactory system more than the taste. This is because there is primary taste, secondary taste, primary olfactory and secondary olfactory inputs; in the end they all will reach the association cortex which is mainly in the medial orbitofrontal and a little in the lateral posterior orbitofrontal where the flavor association cortex is located. Both of them will receive from the taste, olfactory and visual senses. All those related sensations are integrated in the insular cortex (which is a multi-sensation processor) and then there is feedback to primary sensation and secondary sensation cortices.

Remember that the olfaction is much more potent because it works through 2nd-messenger type of receptors compared to the taste pathway which opens direct ion channels.

MEMORY

The memory is a facilitated/facilitator circuit. There are two types of memory in relation to time: working memory (short-term memory: a synapse circulates till another synapse takes its place then it is gone) and long-term memory (requires anatomical modifications). Also memory can be divided into *declarative* and *non-declarative*. The declarative is the nominal memory where you can answer anything directly if you know it like your name, age… While the non-declarative are the things that you memorize without explanation or without answering a question as in classical conditioning (e.g. Pavlov's experiment), writing faster, solving a puzzle and pinning. The declarative memory is mainly stored in the cortex while the non-declarative is stored in the cerebellum.

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