Neurobiology

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Lecture 5.6: Vertebrate olfactory system

Hi everyone, welcome back to Neurobiology. In this series of videos we have been looking at sensory systems and in last two videos we have been focusing on the olfaction, the sense of smell. We have looked at the insect olfactory system in some detail and in this video we will now look at the vertebrate olfactory system. So how this system is organized in our brain or in a mice brain. This will also give us an opportunity to see the similarities and differences between the sensory systems in smaller and bigger organisms. So let's take a look.

Here is a schematic of the vertebrate olfactory system. We smell through the nose, the odors enter the nasal cavity and inside the nasal cavity there is a region of the skin known as the olfactory epithelium. On this part of the skin, the olfactory sensory neurons are present which contain the odorant receptors. The axons of these neurons then go to the brain and in between there is a part of the skull known as the cribriform plate.

So we can look at this region in more detail in this picture here. This is the olfactory epithelium. Here are the olfactory sensory neurons that are present and the axons are passing through holes in the cribriform plate and reaching the brain. The first region of the brain that receives olfactory information is called the olfactory bulb. This is like the antenna lobe in the insect brain.

It is also organized into glomeruli and the sensory neurons provide their information to these glomeruli. From there the mitral and tufted cells which are like the projection neurons of the insect brain carry this information to higher brain areas. And the biggest target of these is the olfactory cortex or also called the piriform cortex. And these mitral and tufted cells go from olfactory bulb directly to the cortex without having to pass through the thalamus. So that was one of the differences we saw in olfaction compared to other senses that information reaches the cortex without passing through the thalamus.

Here we can see the structure of the olfactory epithelium in a bit more detail. So we are looking at the thickness of the skin here. Inside the epithelium we have the olfactory sensory neurons. These are the cell bodies. And then they have very fine branches that come out known as cilia.

These cilia contain the odorant receptor proteins that will detect the odors. There are two other types of cells that are present. One is supporting cells. These cells provide structural support as well as metabolic support that help in maintaining the nutrition for the olfactory sensory neurons. And there are also basal cells.

These are basically stem cells that can form the supporting cells or form the new olfactory sensory neurons. Although most neurons in our nervous system do not regenerate but olfactory sensory neurons are one of the few types of neurons that actually change over the lifetime of a person. The cilia of the olfactory sensory neurons are immersed in a mucus. So odorant molecules that come in through the air that we breathe in get dissolved in the mucus. And they can then either diffuse to the cilia and bind to the odorant receptors or there are also some specialized types of proteins known as odorant binding proteins that are present in the mucus.

They can be thought of as boats that can help in transporting the odorant molecules to the receptors. When the odorants bind to the receptors they indirectly result in opening of some ion channels that changes the membrane potential inside the neurons. And that results in generation of fraction potentials that are carried by the axons of these neurons to the olfactory bulb. Here is an actual image of the olfactory epithelium. And again the cells are very densely packed.

Here is an olfactory sensory neuron. There are some basal cells and some supporting cells inter dispersed. And here we can see very fine hair like structures, the cilia that help in increasing the surface area for expressing the odorant receptors. Now humans have about 350 types of odorant receptors and mice may have almost 1000 types of receptors. Here is an interesting point.

We all know that dogs have a really good sense of smell. Much much better than humans. Can you guess where this difference might be coming from? Well one possible explanation could be in the types of receptors that are present in humans and dogs. So maybe dogs have a much larger number of receptors. But because each receptor requires a dedicated gene, so if dogs had 10 times more receptors than humans then they would also need to have 10 times more genes for coding these receptors.

And that probably would not be feasible. The main difference actually comes from the number of olfactory sensory neurons. Humans have about 5 to 6 million of these neurons that are present in the epithelium. While dogs have almost 50 times more, so up to 300 million of olfactory sensory neurons which express about 800 types of receptors. This number 800 is still much larger than the human receptors which is about 350.

But the main difference comes from the number of neurons. And that is possible because dogs have a much larger olfactory epithelium and also have a more dense packing of the sensory neurons in that epithelium. So in the case of vertebrates also there is a combinatorial coding at the level of receptors. Each odorant activates a subset of the receptors and each receptor is activated by a subset of odors. So by knowing exactly which subset of receptors is activated, the brain can figure out what odor must have been present.

The olfactory receptors of vertebrates were found by two scientists Richard Axel and Linda Buck who received a Nobel Prize in 2004 for their discovery of the odorant receptors and also for figuring out this combinatorial coding at the level of receptors. Normally when the concentration of an odorant is increased, we perceive the smell more strongly. But in some cases something very interesting happens. If the concentration is increased sufficiently, in some cases that might change the perceived odor completely. For example, the chemical thioterpenol at low concentrations smells like tropical fruit.

At somewhat higher concentrations it smells like grapefruit. But at very high concentrations it smells putrid or rotten. Can you guess why this might be happening? When we increase the concentration of an odorant, we would activate some neurons probably more strongly. We would generate more action potentials in them if they were not already saturated. But in some cases we also get activation of extra receptors.

The odorants activate the receptors by binding to them. And the binding probability increases when the concentration increases. And if the concentration is high enough, then we start getting non-specific binding. So at very high concentrations we can get a larger set of receptors activated. So that changes the combinatorial code at the receptor level and it can also change the activity in the olfactory bulb.

There are millions of olfactory sensory neurons present in the olfactory epithelium. And each of these neurons expresses one of the several hundred types of olfactory receptors. So each type of receptor would be expressed in thousands of neurons present at different locations within the epithelium. So let's say orange is one type of receptor and green is another type of receptor and they are present at different regions within the olfactory epithelium. Here we are looking at a schematic of the mouse olfactory system.

Now all the neurons that express the same kind of receptor project in the same regions of the brain. This is the right olfactory bulb connected to the right nose and this is the left olfactory bulb connected to the left nose. As we saw in the case of insects, the sensory neurons project to well-defined zones in the olfactory bulb and these zones are the glomeruli. One small difference here is that in the case of most insects, there is one glomerulus for each type of neuron but in the case of vertebrates there are two glomeruli within the same olfactory bulb. So given the combinatorial code at the receptor level, each odor activates a certain subset of receptors and therefore will result in activation of a certain subset of glomeruli.

So that is sometimes known as the glomerular map of the odors. Now within the olfactory bulb, there are a few types of neurons. There are tufted cells and mitral cells which take information to the higher brain areas and then there are some neurons that are local within the antenna lobe. So we can look at this organization in a bit more detail on this side here.

These are the glomeruli. The axons of the sensory neurons come and project within the glomeruli and there they form synapses with the dendrites of the mitral cells or the tufted cells. But it is not a simple linear transfer of information from sensory neurons to these mitral cells. There are also lateral interactions which are mediated by several types of neurons such as the periglomerular cells and short axon cells that provide lateral interactions at the level of glomeruli and then there are granule cells which provide lateral interactions directly between mitral cells. These lateral interactions are mostly inhibitory in nature. These periglomerular neurons or granule cells are excited by the sensory neurons or the mitral cells and then they provide inhibition back to these neurons.

And these neurons can help in either normalizing the activity of the system or they can help in increasing the contrast. For example, let's consider these two mitral cells. If this mitral cell is firing at a high rate and this is firing at a low rate and these neurons provide input to this granule cell and this granule cell in turn inhibits these two neurons back. Now the inhibition provided by these granule cells may be same for both the neurons. So there might be an equal subtraction of activity in both these neurons which would cause a large fractional effect on this low activity neuron while still allowing the high firing neuron to continue to fire.

So in this way these lateral interactions can result in increasing the contrast between the activity of parallel neurons. Now after the olfactory bulb, the mitral and tufted cells take this information to several higher brain areas. The primary target of this information is the piriform cortex also called the olfactory cortex or piriform cortex which is present in the ventral part of the cortex at the intersection of the temporal and frontal lobes. But there are a few other targets such as the olfactory tubercle, the amygdala. As you might recall from the introductory videos, amygdala is the region that is involved in processing of emotions particularly fear and some people think that this connection explains how smells play an important role in affecting our emotions.

And some information also goes to an area of the brain called the entorhinal cortex and from there this information goes to various other areas like hippocampus, hypothalamus, thalamus, frontal cortex. In the case of mice, there is also an additional sensory organ known as the vomeronasal organ in addition to the olfactory epithelium and the sensory neurons from the vomeronasal organ go to a region called the accessory olfactory bulb. So this is like the olfactory bulb but it gets sensory neurons only from the vomeronasal organ not the main nose. And the vomeronasal organ also expresses olfactory sensory neurons containing olfactory receptors but these receptors are specialized for detecting pheromones. Pheromones are chemicals that are used by a member of a species to communicate with other members of the same species.

These chemicals may be present on their body or they can be released in the environment and can be detected by other animals as odors. These chemicals may be important for sexual behaviors between males and females and for social behaviors for example communication between a mother and a pup or between members of the same family. Pheromones have been detected for many animals including mice and even insects have pheromones. You must have noticed ant trails so ants are able to follow a line because some ants lay down the pheromones and other ants are able to follow those pheromones. Similarly in the case of Drosophila, 11-6-vexinyl acetate CVA is a very potent pheromone.

It is released by male Drosophila flies and it has an attractive effect on females while it repels other males. Now it has been a point of debate whether humans also use pheromones. Some chemicals that are found in our sweat for example have been proposed as possible pheromones but there is no consensus on whether these are actually serving as pheromones. But nevertheless there are several products available in the market that claim to be pheromones to spice up your social life but one must be careful before buying these kinds of products.