Neurobiology

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Lecture 5.4: Olfaction (sense of smell)

Hi everyone, welcome back to Neurobiology. In this series of videos we have been looking at sensory systems. We have looked at the general principles of sensory perception. We have seen the kinds of receptors that are involved and we discussed the idea that the perception is holistic in nature. So there are different stages in the sensory systems at which various features are extracted and we finally perceive some objects. Most of the examples that we have seen so far have been from the visual system.

And that's partly because vision is the most studied sense so far. But in the next few videos I will talk mostly about the olfactory system, the sense of smell. It is somewhat less studied but it is equally interesting. And we will see that it differs from vision in some very important ways.

So let's get started and see how the sense of smell functions. The sense of smell and the sense of taste are together known as the chemical senses or chemosensation or chemoreception. In both of these cases we are detecting chemicals that are present in the environment. So what is the difference between smell and taste then? If both are detecting the same kind of thing. One trivial difference of course is that smelling happens through the nose and tasting happens through the tongue.

But is that the only difference? Well the major difference is in how the chemical is delivered to the sensory organ. In the case of smell we can detect volatile chemicals. So the source of the chemical need not come in contact with us. It can be far away and we can detect volatile chemicals that are coming off that source. But in the case of taste we can only sense something if we come in contact with it.

So taste is also known as contact chemoreception. We have to put the source on our tongue to be able to taste it. There are some more differences between smell and taste. Although both involve receptors that are detecting chemicals, the family of receptors that enable smell and the family of receptors that enable taste are different protein families. So there are some differences in their amino acid sequences.

And also there are differences in the flexibility of behaviors that are associated with these senses. We can detect a large number of smells and the behaviors that we associate with those smells can be quite flexible. We can like or dislike smells and we can change those preferences quite flexibly. Whereas in the case of taste, the preferences associated with the different tastes are somewhat more hardwired. So we have already discussed earlier in the course that the sweet taste is preferable to most people.

Bitter tastes are not preferable. Similarly, low salt concentrations are usually preferable but high salt concentrations may not be preferable. And although there is some flexibility in these behaviors also but they are somewhat more difficult to change compared to the smell. As we all have experienced, we can perceive many different smells or odors. These smells are produced by different chemicals or odorants and these chemicals can come in an almost infinitely large variety.

These chemicals can differ in their molecular composition, in their shapes, sizes, the side chains, the functional groups that they have and any such variation can possibly change the smell of the compound. Now the number of possible odorants is therefore almost infinitely large. But it happens that many times different molecules can result in similar smells. So the number of different smells that we can perceive is going to be smaller than the number of possible molecules. And how many different smells we can have is somewhat of a debated question.

One paper published a few years ago came to the conclusion that we can have trillions of smells but that was based on an extrapolation. So it is still debated. But everyone working in the field would agree that there are at least several thousands or millions of smells. What further adds to the complexity of smells is that many of the common smells that we perceive are not based on a single compound but many compounds coming at the same time. So the aroma of coffee that you had recently could have been produced by dozens or hundreds of different compounds.

The sense of smell is quite different from the sense of vision. There is one way in which it is more complicated than vision and there is one way in which it is more simple than vision. See if you can guess which are the two ways I am referring to. Smell is more complicated than vision in terms of the dimensionality of the input. So in the case of vision the input is light and the light can be quantified in terms of its intensity and in terms of its color.

The color can be defined in terms of three axes, red, green and blue and therefore we just need three types of receptors. But in the case of olfaction the inputs are the different chemical molecules and the shapes of these molecules can vary in many different ways. So it is not possible to define three or four or a few parameters on which all the shapes can be described. And the result of that is that we need to have many many different types of receptors to be able to detect the different chemical molecules. So we have hundreds of receptors for the sense of smell as opposed to only three types of receptors for the sense of vision.

The way in which the sense of smell is simpler than vision is in terms of the spatial complexity. When we see things we can detect the color of light coming into our eyes from many different locations in space at the same time. Each point in our retina gets input from a narrow receptive field, a particular region of space and therefore our brain is able to figure out how the colors are distributed in space at any instant. But in the case of olfaction at an instant we only get one smell. We do not have this detailed information about the smells coming from different locations.

Now to some extent we may be able to figure out the source of the smell if we move around or if we compare gradients of smells over time. But that requires extra effort and still is possible only to a very limited extent. But at a given instant we only get one smell. So we lack this rich spatial information that is possible in the case of vision. And there is one architectural difference between vision and olfaction.

So in the case of vision as in most other senses the information from the sensory organs reaches the thalamus and then it goes to the cortex. But in the case of olfaction the information from the sensory organ that is the nose goes directly to the cortex without going through the thalamus. The sense of smell is not unique to humans or higher organisms. In fact it is one of the most ancient senses and is present in a large variety of organisms. The reason that flowers have smell is not to please humans but to attract insects.

So that they can come and pollinate the flowers. So the tiny insect brain that may have only about 100,000 or a million neurons has a reasonable portion of those neurons devoted to the sense of smell. And even simpler organisms like the worm C. elegans which has only about 300 neurons in its brain also has some neurons devoted to detecting volatile chemicals in the environment. As we have been seeing throughout this course studying simpler organisms can provide us lot of valuable insights into how the human brain works.

And that has also been the case in the case of the olfactory system. So a lot of insights have been derived by studying the brains of insects for example. In particular honey bees, Drosophila, cockroaches, locusts and moths have been used quite extensively to study the olfactory system. And the advantage of studying these simpler organisms is that they have a relatively smaller number of neurons. So it is possible to study them in sufficient detail and it is possible to do various kinds of manipulations on these small brains that would not be feasible or ethical to do in larger organisms.

And also the organization of the insect olfactory system is quite similar to the organization of the olfactory system in our brains or in the mice brain. My own research has also been in the insect olfactory system. During my postdoctoral years at NIH, I started working on the locust olfactory system. And now my lab at IIT Kanpur works on olfaction in mosquitoes and fruit flies. Let me give you a glimpse of how these kinds of experiments are performed.

So we are looking at a locust here in this picture from top. You can see its legs, its body and the head here. And from the head we can see two antennae coming out. The antenna basically serves as the nose of the animal. The receptors are located on the antenna and then the axons of these receptors go into the brain inside the head.

If we want to see how the neurons in the brain are responding to smell, we normally have to do a small surgery on the head of the animal. And to prevent the head from drying up, we make a small wax cup around the head and fill that wax cup with some saline solution that matches the fluid that is present in the body of the animal. So this is what the preparation looks like. We have a wax cup around the head and it is tightly sealed around the body so that the saline cannot leak below. And the head cuticle has been cut with very fine blades and we can see the brain here.

A small metal pin has been inserted below to support the brain as you can see here. So now this brain is accessible. This small structure here, in the case of locust, it is about 1 mm in diameter. It is exposed and now electrodes can be placed in the brain. So we can give some odour to the antenna using a small tube through which odours are being puffed and then we can see how the neurons in the brain are responding to this odour puff.

So on the antenna here, there are olfactory receptor neurons that are located and these olfactory receptor neurons send their axons to an area of the brain called the antenna lobe. So this is the first olfactory processing centre in the brain which contains two types of neurons, projection neurons and local neurons and then these neurons project to higher areas. Just like humans, insects can also smell a very large number of chemicals. So the number of possible odorants is quite large for them also. Just for argument's sake, let's say that number is 1 million.

So how many different receptors would we need to detect 1 million odorants? If we assume a one to one mapping between odorant and receptors, that is if we assume that for each unique odorant we have a unique receptor, then we would need a million receptors and of course that is not going to be feasible because that would require us to have a million genes and a typical animal has only about 20,000 or 30,000 genes in total including every cell of the body. So clearly a one to one mapping between receptors and odorants is not feasible. The solution that nature has adopted is a combinatorial code at the level of odorant receptors. By that I mean that there are still many different receptors but now these receptors are not unique to odors. Each receptor can be activated by multiple odorants.

So for example this first one here is activated by this odorant, this odorant and this odorant among this set of odorants and this second one here is activated by these two, this third one here is activated by these five and so on. And similarly each odorant can activate multiple receptors. So this odorant here let's say activates this set of receptors and a similar odorant with just one extra carbon activates a slightly different set of receptors. And by reading out this pattern of which set of receptors are activated the brain can figure out which odorant must have been present. So this is the idea of combinatorial coding.

So if we have K receptors we can potentially encode 2 to the power of K different odorants by looking at all possible combinations of these receptors. So this kind of coding allows a reasonably finite number of receptors to encode a very very large number of odorant molecules. Thank you.