Cognition and its Computation
Prof. Rajlakshmi Guha
Prof. Sharba Bandyopadhyay
Biotechnology and Bioengineering
Indian Institute of Technology, Kharagpur

Lecture - 32
Cholinergic System, Bottom up and Top down

Welcome. So, we have been discussing the neurobiology of attention and working memory and how neural representation is changed through sensitivity control mechanisms. And, in that discussion we had said that we will talk about the bottom up saliency filters in the next lecture. And so, let us remind ourselves about the framework of attention or the elements of attention that we had discussed in the previous lecture.

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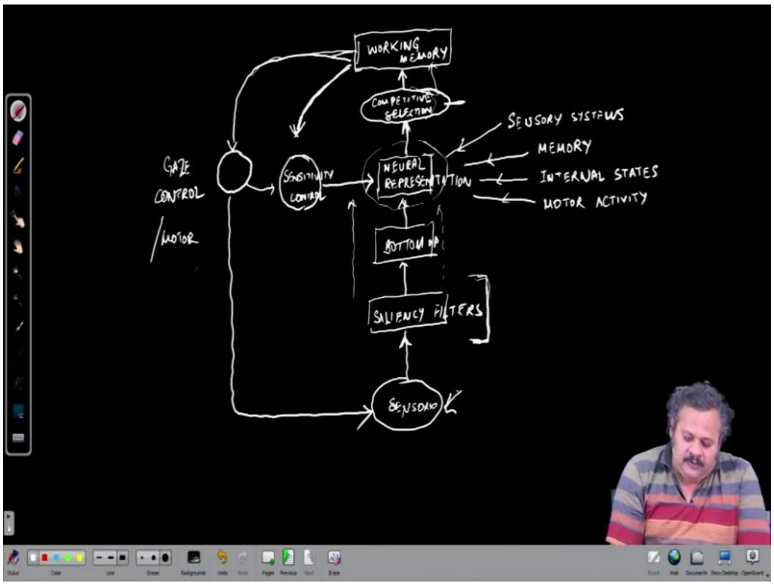

And so, as you can see we have the external sensory world, this is the external sensory world. And, we have something that we call the bottom up saliency filters, then a bottom up representation as we have learnt in the sensory circuits then, a representation of the higher order representation of the surroundings like objects and so on. And, then competitive selection based on relative saliency of the objects and which goes into working memory and then these direct sensitivity control which changes the neural representation.

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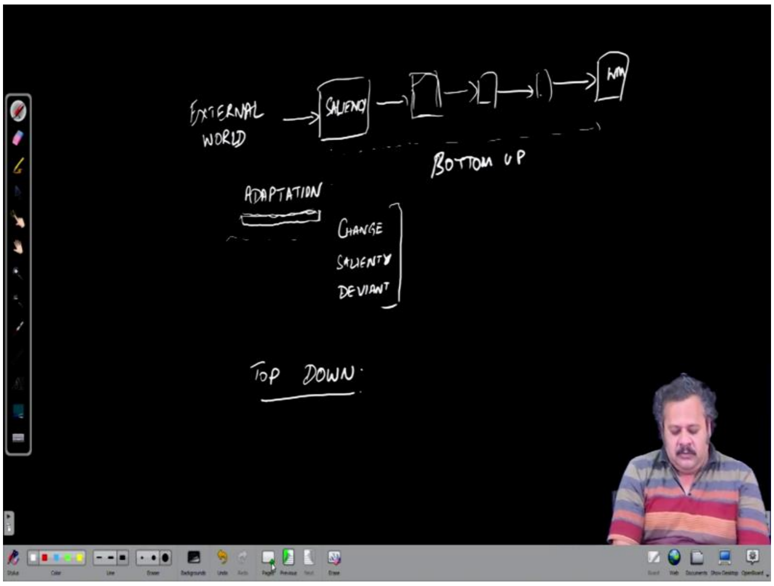

And so, when we talk about the saliency filters, what we mean is basically in our external world we are being constantly bombarded with stimuli. I mean it is a dynamic situation where the variety of stimuli are constantly coming in through our peripheral sensory receptors. And, we tend to focus only on a few particular elements at a time and that is what is in the working memory.

And, sometimes in the overall bottom up representation, particular salient sounds, not sounds salient stimuli themselves create make their way into working memory. We may or may not so, that is what we mean that bottom up saliency filters. The stimuli by virtue of their salience, we after with the neural representation bottom up neural representation past comparative selection way into working memory.

So, how this happens is that the stimulus the filters that we have in the periphery and as we go up the pathway the sensory pathway, a common feature of neurons is adaptation. And so, we tend to adapt to something that is continuously happening and all of a sudden a change or a salient event in the stimulus world salient event or deviant event that is out of the expectation that does not match with what we are inherently expecting at the current situation.

When such a stimulus occurs, it bypasses this I mean it is not a stimulus that is not in a situation that it would go through adaptation that is there are synapses that are not adapted. Remember, we talked about short term plasticity where we had depression, short term depression and throughout the pathway the synapses adapt or rather depressed in the short term.

And, that is what reduces our responses to the continuous ongoing environment that we are adapting to continuously. And a deviant stimulus, a change from that situation causes increase in activity in synapses that are not present, that were not previously active. And so, that is what causes a strong response to this changed event and that is what we mean by saliency filters and it immediately goes into the working memory region.

We may or may not continue to keep it in working memory. But, these distractions or these salient events depending on the context may or may not stay in our working memory. For example, if right now if you have a knock on the door and you know that there is nobody outside you know from this room, then it is a change from the current situation.

And, that will go into working memory and I would maybe be stop depending on the situation maybe stop and go and see if there is an emergency or if there is all of a sudden a siren in the building, that will immediately go into my working memory and actually modify how I do like take the next steps and change our planning. And, again there may be a simple door slamming shut and that also is a salient event that will work through the throughout the pathway.

And, I will momentarily pay attention to that, but then it will die away immediately as I move back my focus on to this lecture. So, depending on the situation these saliency filters in the environment in the bottom up circuitry that is inherently there from the adaptation mechanisms of synapses plays a role in attention.

So, this is a bottom up effect of a bottom up component of attention. The others that we have been talking about that is the sensitivity control that is really. So, this is the bottom up side and what we have been talking about is essentially top down control that is from the prefrontal cortex.

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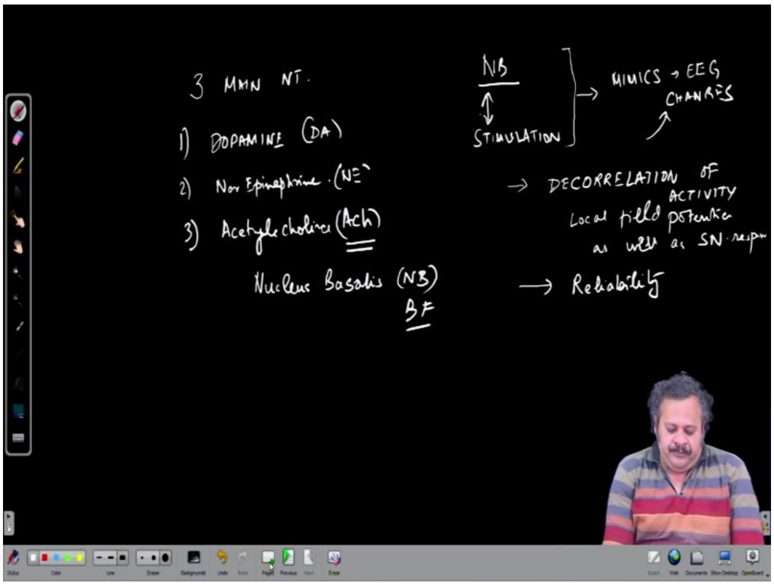

So, in these ways in the top down process and in general in attention there are three main neurotransmitter that are involved, but one is dopamine that is DA. So, prefrontal dopamine plays a big role in attention, 2 is nor epinephrine or NE and possibly the most important among them is acetyl choline or ACh. Profound role of ACh or acetyl choline is known in attention.

And, we will talk about that particular structure which is as we know is the nucleus basalis or the in the basal forebrain, basal forebrain that gives diffuse projections throughout the cortex, diffuse cholinergic projections throughout the cortex. And, there are both nicotinic and muscarinic acetyl choline receptors.

What I mean by nicotinic and muscarinic is if you remember from our lectures on synaptic transmission, nicotinic is the equivalent of ionotropic transmission for acetyl choline as the neurotransmitter and muscarinic is the metabotropic receptor of acetyl choline. So, muscarinic receptors and nicotinic receptors both are involved in this process.

So, first of all this is this shows how the nucleus basalis comes into play. First of all is that if nucleus basalis is stimulated electrically, nucleus basis stimulation rather the arrow that way; this mimics the effects of attention in the in terms of the local field potential or EEG signals. The EEG changes when attention when we focus there is an increase in the high gamma 50 to 100 hertz gamma region.

And, nucleus basalis stimulation also shows similar changes in the EEG of an animal. Secondly, nucleus basalis stimulation also leads to decorrelation of activity, which is what leads to actually the changes in gamma the decorrelation of activity in local field potential as well as single neuron responses, single neuron responses. It also causes reliability in responses.

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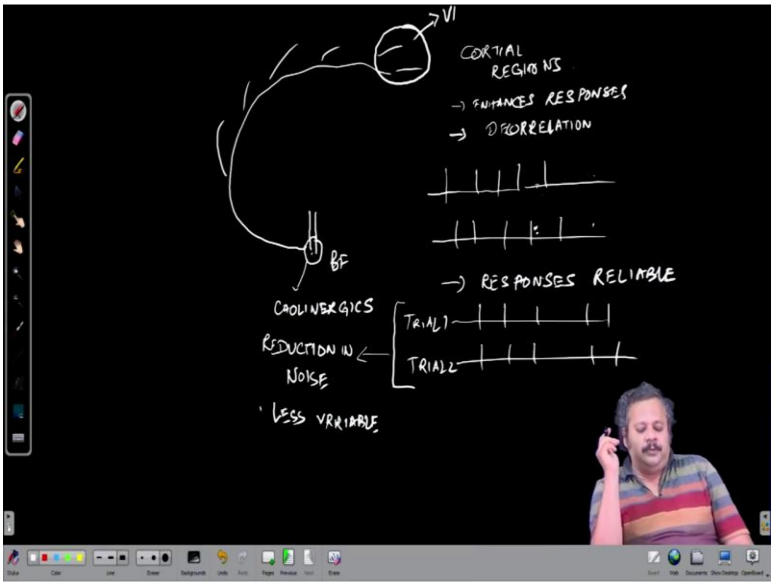

So, we will talk about some of these in a little detail. So, these are experiments done in mice where the nucleus basalis region which are which contain the cholinergic neurons. This is the basal forebrain let us say, it has the cholinergic neurons that is neurons that have acetyl choline as their neurotransmitter and it projects diffusely throughout different cortical regions so, from the basal forebrain into the cortical regions, different cortical regions.

So, what is found is that if we have a stimulating electrode in the nucleus basalis and let us say we record from the primary visual cortex V 1, as you remember from the visual lectures. The effect of the stimulation on responses of V 1 neurons to presentation of stimuli show all the three features, that we talked about.

First of all, it enhances responses to the preferred stimuli of the neurons. It provides decorrelation that is single if we consider the spiking activity of a neuron in V 1. And, another neuron, pairs of neuron in this manner and compute how correlated their activities are by seeing how well their spikes are synchronized. Then, we find that they are less synchronized when the basal forebrain is activated or stimulated.

However, on different repetitions, so, this is decorrelation. So, how would the decorrelation be useful in terms of coding or representation of the stimulus? It basically allows build increase in capacity that is much more information. So, less redundancy will be there across the different neurons in terms of what information they are carrying. And, also the when stimuli are repeated from trial to trial, then responses become more reliable.

So, with basal forebrain stimulation, if we have stimulus being present again and again then the spike times of a neuron tend to be at same or similar time points across different trials. So, this is trial 1, this is trial 2 and so on. So, this means that this reliability means that there is reduction in noise or variability of responses. So, less the variability less the variability; obviously, the better is the representation of the stimulus.

So, nucleus basalis thus we are; now, we have been talking about this as if we are you know we are artificially not as if we are artificially stimulating the basal forebrain, as if that attentional processes would be stimulating the basal forebrain. And, there are studies that can be shown that actually if we have shown, that if we actually turn off the nucleus basalis inputs into V 1, then animals in this case mice tend to perform poorly in attentional tasks.

And, the tasks that require more attention, they tend to perform poorer in those cases than in cases, where the animal does not require as much attention that is easier tasks. So, similarly if we in a behaving animal if we activate the basal forebrain, it actually improves the animal’s performance.

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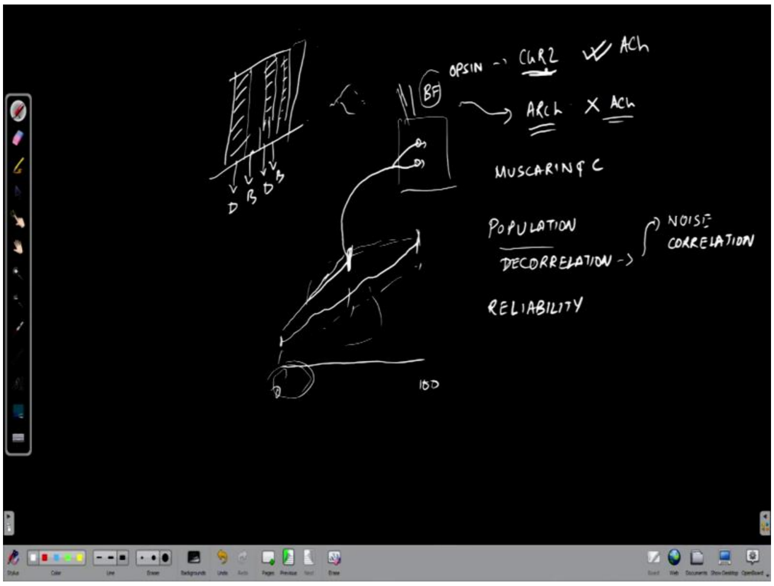

So, this is how the experiment goes, that is in screen in front of an animal, in this case of mouse as we were saying there are bars of light appearing at a particular orientation. So, the animal has to distinguish between two different orientations either the vertical or the horizontal for different levels of contrast. So, this is dark, this is bright, this is dark, this is bright and so on.

So, if we reduce the contrast to nearly 0, it becomes all gray and as we increase the contrast to the highest contrast, the task difficulty decreases; that is it becomes more and more easy for the animal to perform the task of discriminating the orientations in of the stimuli with contrast. So, the way the experiment was done is specifically in the basal forebrain cholinergic neurons opsin, that excites the neuron is generated is expressed.

And so, that opsin is expressed this is particularly channel load opsin as we had discussed earlier on in our lectures on measurement and manipulation of circuitry. So, there are the terminals that go of the basal forebrain neurons that go into V 1, those terminals also contain this channel rhodopsin. And so, if we shine light here, we can actually activate these terminals, the cholinergic terminals and that will lead to release of acetyl choline in V 1.

Similarly, in another set of experiments they expressed arch or a particular kind of opsin that turns off. So, this is enhances release of acetyl choline in this particular case and here with activation of light of particular wavelength, it turns off release of ACh ok. So, during the task for different levels of contrast, let us say 0 to 100 is the scale of contrast; the animal's performance can be monitored as to how well it is able to discriminate the two across the different levels of contrast.

So, if this is the case where the animal's normal behaviour goes, then with the acetyl choline stimulation the performance actually improves in these cases in the intermediate cases. And these cases are obviously, too difficult where we have extremely poor possibility of discrimination because of very low contrast. And, at the highest intensities or highest contrast the task is easy and so, does not require that much of attention in the performance.

And so, with the stimulation there is no room for improvement. So, in the intermediate cases there is improvement in the performance. And, similarly for the acetyl choline block that is when we are stimulating with light when the animal is performing the task and arch is expressed in these terminals, in the basal fore neurons and hence the axon terminals in the primary visual cortex; then the performance from the normal actually gets poorer.

And so, this particular experiments, experiment shows us how casually the basal forebrain or acetyl choline is related to attention in particular visual tasks. So, this can be generalized with further experiments and further conclusive causal experiments into other sensory systems as well. So, in this experiment also the same effects of nucleus basal stimulation were observed where in the optical stimulation was done.

That is increased reliability of responses and decorrelated activity, increased gamma, these are all effects of attention that are mediated through these cholinergic inputs. Secondly, another conclusion from the study showed that it is primarily the muscarinic receptors in the visual cortex. It is the muscarinic receptors in the visual cortex that are involved in this particular attention, in this particular way of control of activity by the nucleus basalis or the cholinergic inputs.

So, in this particular case, they also studied what happens in the thalamus which is below the primary visual cortex thalamus, were in the LGN from where, inputs to the V 1 goes and the nature of changes is different. And so, this is more of a phenomena that happens in the cortex and different effects can be happening down the pathway, that is in the bottom up representation there are changes from this attention, but of a different kind.

So, it is not that the sensitivity control is happening only at the level of the full object, it is happening in this case V 1 is quite low in terms of object recognition pathway. So, we are seeing effects in V 1, similarly there are effects in LGN also. And, there are studies where more of the dopamine is involved in visual spatial attention in the frontal eye field which is in V 4, where people have shown that it is based on dopamine.

Again, a contrast based enhancement can be seen in terms of the direction where we look and recept, if the direction where we look is controller of that movement in the frontal life field, if that is stimulated; then the representation of a preferred stimulus in that particular location in V 4 which is a higher order visual area, the representation gets enhanced. And, the representation gets poorer in the non-preferred locations.

So, again a contrast enhancement kind of change is seen in the visual spatial attention as well. So, in sort of summary as we have gone over a few examples of attention, we can say that the effects of attention are in terms of one in case of attention is through enhancement of preferred stimuli and suppression of the surround that is the contrast change. Secondly, it acts through population of neurons by decorrelation, decorrelation of activity.

And, thirdly it is also reducing the noise so, to speak by making responses more reliable. So, not only enhancement, but also reliability in terms of the representation becomes stronger in that sense, that there is less noise across the population for the next level circuitry to gain information out of the out of the lower level and that reliability helps in decoding that activity.

The there is further another thing, that also is mediated by acetyl choline as has been studied in primates primarily and it is related to this de correlation. And, that has to do with again at the population level what we call noise correlations. So, we would not go into the detailed mathematics involved in that. What it essentially means is how functionally connected pairs of neurons are. So, we will talked about decorrelation in the population responses.

And, noise correlations is similar, it only shows that how functional connection, it is a poor measure, but still it reflects the functional connectivity between neurons. And, lowering of noise correlations in general with increasing responses to the stimulus helps in decoding information based on the population of neurons. And in fact, there are studies that have shown that this particular phenomena play plays a very strong role in terms of the decoding performance of neurons.

And, it is still I mean although the evidence is quite strong; there are further conclusive causal experiments that need to be done in terms of the noise correlation effects. And, to conclusively say that it is the most important event of or most important part of attention. So, with this we will end our lectures on attention and next we go into more of the object recognition and visual scene analysis and so on.

Thank you.