Cognition and its Computation
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Lecture - 44
Developmental Plasticity/Learning/Critical Period

Welcome. So, we have been talking about functional and structural plasticity and we ended our discussion on structural plasticity alluding to how big bigger role structural plasticity plays in development.

So, during development I mean if we start from the very beginning from the neural tube there are many many steps that occur until the form of the cortex that we see is reached or form of the brain we see is reached at least in overall broad structure and the bigger structure that should be present they appear and at the entire brain is formed which is much later during gestation.

And on birth perinatally, there are more changes that keep on happening and actually these kind of changes continue on for a few years and sometimes in some parts of the brain for many tens of years actually in the frontal cortical regions for example. So, these kind of changes structural changes during development initially are controlled by many of the molecular cues that actually govern the course structure formation that is as like we have talked about earlier the different pathways.

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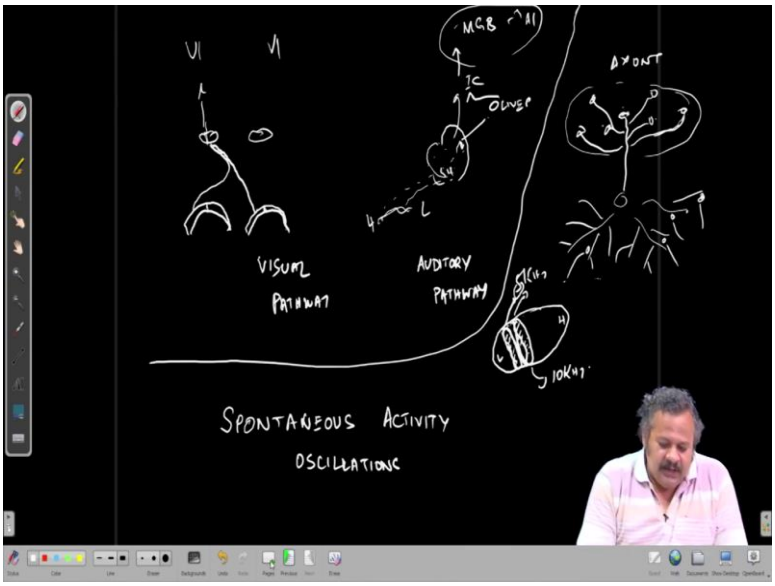

When we think of the visual pathway let us say or even the auditory pathway we know that in the visual pathway there is tremendous specificity. So, if we think of the retina this particular region the two different eyes, the different halves of the retina we have the images of the different the two different hemi fields in the two different sides of it and then they project on to the LGN and the LGN onto V 1 in the cortex.

So, this entire pathway from the retina to the LGN to the V1 these connections need to form very precisely and as we say as we know let us say this region is connected to this region and similarly this region is connected to this region. And the two sides actually register similar locations or same locations or almost nearby locations on the retina or the in from the visual field onto the same column within the LGN as we have discussed.

So, think about the developing system when the retinal ganglion cells are projecting to the LGN how does it know where to connect and similarly the LGN, then projects onto the visual cortex and the retinotopy map is maintained.

And so, that again needs some supervision in terms of how to how the actions go and make connections in the visual cortex in the or even how does the primary visual cortex know that I mean that it is the region where the where the LGN projections need to go and that too in layer 4 even specific parts of layer 4 specific sub parts of layer 4.

So, these are different a set of events that happen in forming the core structure and these are totally guided by molecular cues and controlled by precise on and off turning on and turning off of specific genes and then proteins and actually molecules that are guiding the axons to particular locations in the brain.

So, the similar things are there in the auditory pathway also if you think of the tontopic axis, we know in the cochlea or in the basilar membrane one side has low frequency and high frequency the other side has low frequency and that sort of structure that sort of arrangement of low to high regions is present in the cochlear nucleus. Then also in the inferior colliculus and the olives which is branch out here which again projects to the IC then on to the MGB the thalamic region and then A1 the primary auditory cortex.

So, here we have specially segregated regions that have high frequency selectivity to low frequency selectivity of neurons. So, auditory nerve fibers of high frequency must connect to the high frequency region of the cochlear nucleus. So, here again as we said that these are defined and controlled by specific genetic programs within the system that has evolved in order to establish this circuitry this overall broad circuitry.

So, what we are talking about here is that initially to get the broad structure, it is essentially genetics and it is through guidance molecular guide I mean axon guidance cues which are specific molecules or proteins that are generated which attract the axons or repel axons I mean both are at play in order to create the circuitry where the finally, the axons go and make connections.

However, inside that if we come down one level in the beginning the axons are actually projecting to make if we think of this as an axon, we have been typically drawing an axon with maybe a collateral like this and two collaterals making a synapse here and here. Actually way more synapses are formed by the axon the axons branch initially to many to form many many diffuse connections with many neurons.

And so, from this big overall picture that we were seeing that the circuit is forming from different structures different nuclei up to the cortical regions, if we go one level deeper we find actually that even though the circuit the broad circuit has formed the fine details are totally diffuse in the sense that these axons are like a tree right now I mean making many projections. And similarly the dendrites also are making many many I mean many neurites are there and so, they also receive many inputs initially.

So, this sort of tells us that there are in structural plasticity also there are two stages where one is where the broad connections are made and that is over on this side which we do not really consider in terms of structural plasticity although it may be technically. So, but it is when synapses have formed and that synaptic plasticity is involved that these dendrites are getting input from other axons or other neurons and they gradually get pruned or refined over development.

So, the these get retracted and I and form or form new connections and that is controlled mainly by activity and that is spiking activity as we know. So, given this kind of broad diffuse connectivity profiles in the beginning of the of development, we see a period of activity dependent plasticity. And there are ideas of period even before the stimulus driven plasticity, there is spontaneous activity networks spontaneous activity which are oscillations usually that play a role in defining a finer connections that is.

For example, very recent work over the last decade has shown that like in the inferior colliculus and in a one there are spontaneous activity calcium waves spontaneous waves within A1 and the spontaneous waves are synchronized in regions or synchronized between neurons that turn out to be neurons in the particular frequency region.

So, during development the spontaneous activity if let us say this is the surface of A1 and this is the low frequency side this is the high frequency side, what people have observed is that there are bands of spontaneous activity that are happening simultaneously in this particular region and may be also in this particular region. When the and in this is before the animal actually has sound driven activity that or can have sound driven activity at this period of time.

But it is true that later on with gradual development this particular frequency regions turn out to be of similar selectivity let us say this is 5 kilohertz region and this is all 10 kilohertz region or so on. So, these regions had spontaneous activity together and these regions had spontaneous activity at a separate time in a synchronized manner and so, this kind of spontaneous activity also plays a role in the refinement of these structures of these synapses or these dendritic trees and axonal outputs. Finally, with activity with actually stimulus driven activity with strong stimulus driven activity.

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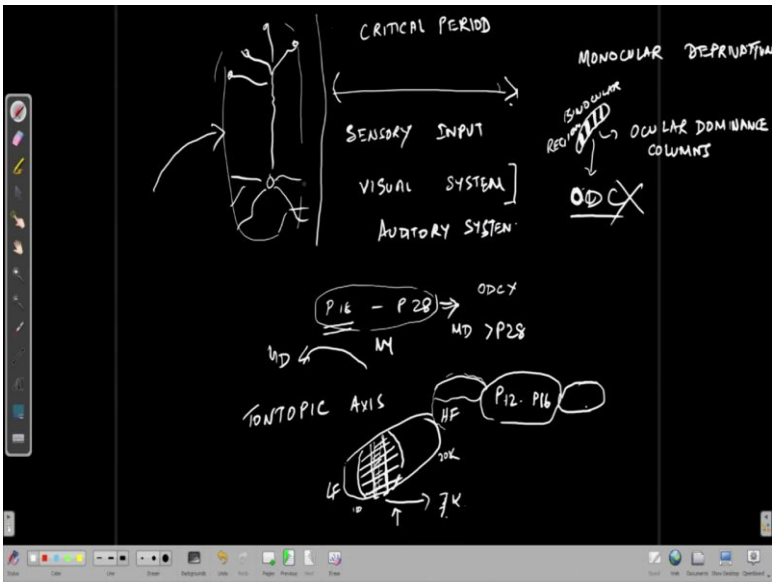

We have more refined structures that are created where the axons project to their final sort of few connections that they are making and the dendritic arbors are also become more stabilized. And this the process of this occurring is thought to be in a period which is what we call the critical period.

So, there are a quite a few studies about such critical period and the ideas behind critical period is that it is a period of tremendous plasticity or immense structural changes in the connections of neurons or huge amount of refinement occurs in these in this kind of this particular period of time.

And it has a particular window of development window during development and manipulations in this particular period of development with the sensory inputs or even now we are seeing similar kind of critical periods appearing even for the frontal cortical regions sensory input manipulation during this period changes the development of the circuit completely.

So, this has been shown very well in the visual system and also in the auditory system where for example, in the visual system in mice or even ferrets and cats all many different species these experiments have been done where actually monocular deprivation is done. So, that is one eye is covered or switched in that particular period of time so, that particular eye does not get any inputs.

So, if you remember from our visual circuits lectures there is a region that is a binocular region in the visual cortex that is getting inputs from both eyes and we know that there are ocular dominance columns there. This particular structure whether there is a separate monocular and binocular region more of the mouse ocular dominance columns and so, basically let us say the white region is selective or responds to the right eye the dark region responds to the left eye and so on.

And if you remember that within hyper columns there are many; there are many ocular dominance columns and within each of those we have orientation selective fields orientants orientation columns many different kinds of orientations and all the other kind of features that the or visual system extracts, they are present in each hyper column.

So, when the system or when the visual system is devoid of input from one particular eye these ocular dominance columns do not form OD columns do not form and as you can see. So, basically that eye becomes basically useless dysfunctional and because the related machinery in the hyper column that is connected to those ocular dominance columns or to which they belong those are all taken over by the other eye which was not deprived of any visual inputs.

So, now what makes this a critical period is that if you do the same procedure of monocular deprivation before the critical period or after the critical period, then this kind of permanent change does not happen that is let us say in the mouse there is a critical period of during P 18 to P 28 where P stands for P natal postnatal sorry that is number of days postnatal day 18 that is number of days after birth.

So, if the monocular deprivation is done within this period actually it can be a little shorter, if the monocular deprivation is done in this period then the ocular dominance column formation is disrupted. But if the MD is done post P 28 that is greater than P 28 then there is no change in the formation of ocular domain columns if it is done for the same amount of time. Similarly, pre critical period if we do the Monocular Deprivation or MD then there is no change in the ocular dominance column formation.

So, that such kind of changes or such kind of permanent changes occur during a particular period of time only that is what makes it a critical period. However, gradually we are trying to see it is that such changes can still be induced later on to a lesser degree and may be to even a higher degree if we can induce a critical period later on through

some molecular mechanisms. So, in the similarly in the auditory system kind of critical period that has been talked about is over expansion of frequency representation as you know.

And as we just discussed the tontopic arrangement in the auditory cortex tontopic axis being present in the auditory cortex let us say this is the surface of the auditory cortex where this is the low frequency side the high frequency side. And let us say we have 100 hertz to 20 kilo hertz here and let us say during a particular period which in the mouse is P 12 to around P 16 during this period what many studies have shown is that if a particular frequency is presented continuously for during this period of let us say 7 kilohertz.

Then if a normally developing animal has a tontopic axis that is as shown where the 7 kilohertz is this band right here then an animal that is exposed to 7 kilohertz over the critical period has an expansion of the 7 kilohertz region. So, this whole region becomes selective to 7 kilohertz at the cost of reduction in representation of this nearby other frequencies.

And so, what this also to this we can also add the fact that if we do this same kind of exposure to 7 kilohertz before P 12 or after P 16 then such kind of permanent changes do not happen.

So, that makes this period that is crucial in terms of development in terms of this activity dependent refinement of the synaptic structures or the entire network structure from the diffuse architecture that we had talked about to become this refined kind of circuit that ultimately works for most part of the life and with minimal reduction in structure or less reduction in structure.

So, the other aspects here is that we can actually delay the period of critical period through again activity. So, these are all experimental evidences that we still do not have complete computational models to explain is that like in the auditory system if we remove.

If we present the animal in this case mouse or rats in which the experiments were done if broadband noise is presented throughout critical period then let us say up to P 15 instead of P 16. And then the critical period actually gets delayed by that much which is a very

very interesting phenomena and so, the critical then after the noise presentation one can then do experiments where you present a single frequency and there is an expansion of that frequency.

So, the critical period is moved further down the line. Similarly, visual deprivation complete deprivation in the critical period leads to a delay in the critical period. That is if we deprive the visual system of any light during the original critical period that is during the period where when with activity it is supposed to change its structure the synapses would be refined or the dendritic T trees would be refined that does not happen during that period, but happens after the visual deprivation period is over and when it gets visual activity it starts.

So, there are basically activity dependent cue cues for the onset of critical period as well as there must be activity dependent cues for the offset or the stopping of critical period. And so, that so, this makes the system even more complicated in the sense that there are periods of enhanced sensitivity in the formation of the structure of the circuits in the brain and so, some of these aspects have been reproduced by computational models with functional plasticity itself.

However, the other additional aspects like the represent the representation of noise delaying the critical period and so, on are not completely understood computationally although there are a fair bit of ideas about how molecular events can control these particular kind of periods where we have one set of critical period that gets delayed due to some presentation or lack of stimulation and so on.

So, as we saw here we sum up this discussion on plasticity showing you that there is more beyond what we have mainly talked about in our learning and plasticity lectures and that learning itself can have produce changes in structure of the networks it depends on the kind of learning that is happening.

And so, these are areas which have not been completely abstracted down to the level of computational models fully or as convincingly as the other kinds of learning and plasticity models. So, since the network itself is changing it becomes slightly difficult and to come up with rules as to how these changes are being controlled by activity.

So, we end our discussion on structural plasticity during development and the critical period and we stop here and in the next lecture, we will be discussing basically disorders of plasticity that is when synaptic plasticity is dysfunctional because of different changes which lead to different neuro psychiatric coditions.

Thank you.