Introduction to Brain and Behaviour
Professor Ark Verma
Department of Humanities and Social Sciences
Indian Institute of Technology, Kanpur
Lecture-24
The Medial Temporal Lobe Memory System

Hello and welcome to the course Introduction to Brain and Behaviour. I am Doctor Ark Verma from IIT Kanpur. This is the fifth week of the course and we are continuing to talk about the medial temporal lobe memory system.

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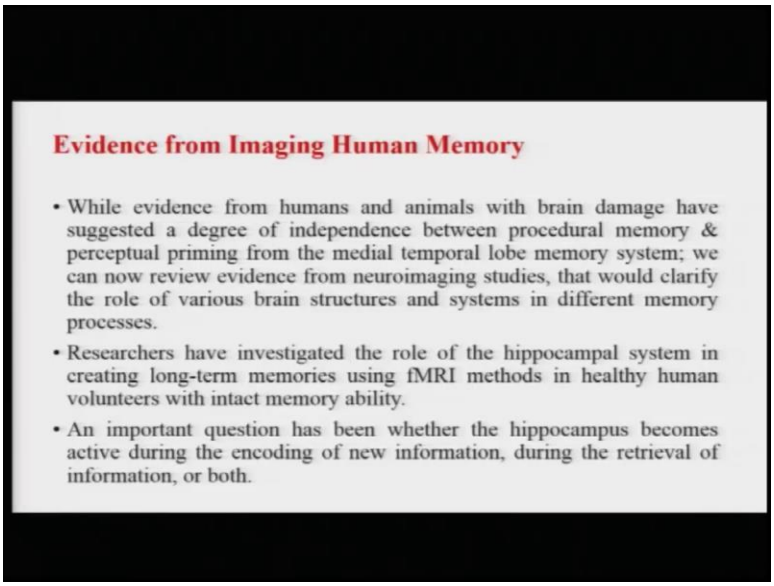

Now, this is the third kind of evidence that we are talking about continuing from the last lecture. Now, a lot of evidence about the involvement of this medial temporal lobe basically comes from neuroimaging studies. Now, neuroimaging studies if you remember neuroimaging basically involves methods like fMRI and PET which allow us to actually scan or which allow us to actually observe the working of the brain in normal individuals while they are still performing particular cognitive task.

So, while evidence from humans and animals with brain damage have suggested a degree of independence between procedural memory and perceptual priming from the medial temporal lobe memory system, we can now review evidence from neuroimaging studies that would clarify the role of various of these brain structures and systems in different memory processes.

So, this is basically what we are going to do in this current lecture. Now, researchers have investigated the role of the hippocampal system in creating long term memories using fMRI methods in healthy human volunteers who also have intact memory ability. An important question can be asked that can be asked is whether the hippocampus becomes active during the encoding of new information or during the retrieval of the new information or that hippocampus's basically useful both in the encoding and retrieval of new information. So, let us look at some of the evidence.

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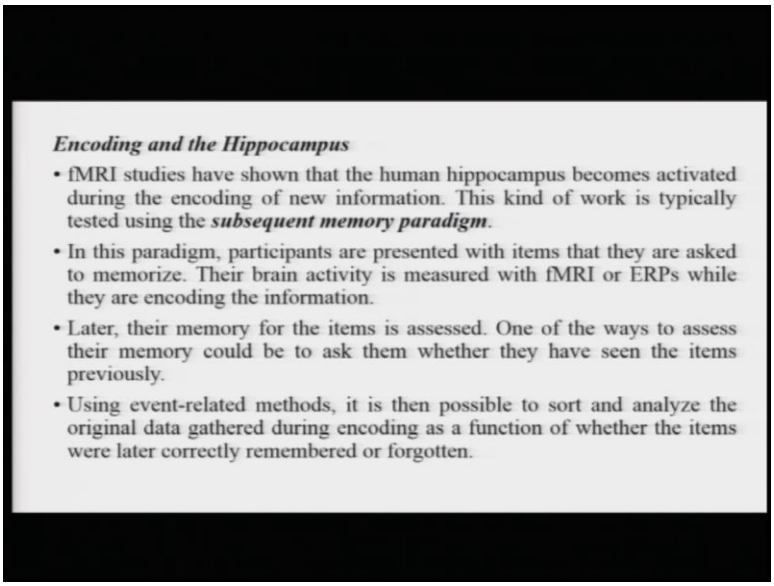

Let us first talk about encoding and the hippocampus. Now, fMRI studies have shown that the human hippocampus becomes activated during the encoding of new information. This kind of work is typically tested using the subsequent memory paradigm. In this paradigm, participants are presented with items that they are asked to memorize. Their brain activity is measured with fMRI or ERPs while they are encoding or learning this information. Later, their memory for these items is assessed. One of the ways to assess their memory is just to ask them whether they have seen these items before.

So, I can present to you a list of words or you know few pictures or objects and I can show them to you and I can ask them ask you to memorize them. Later after a gap of a few minutes or few hours maybe even days I can ask you with a set probes which will have say for example some of

these old items that you actually had seen and some new items that I just randomly mix them together and I ask you whether you have seen this before.

You can tell me with confidently whether you have actually seen this so that you will recollect so that you are recollecting this from the initial episode or you can just say I am not sure whether I have seen this in the list that you showed me but I am familiar with these items. So, these are the two ways in which participants typically respond in this subsequent memory paradigm.

Now, let us go further using even related methods it is possible to sort and analyze original data during encoding as a function of whether the items were later correctly remembered or forgotten. So, based on whatever the participants are telling that okay I have seen this item, I have not seen this item, I am not sure whether I have seen this item you can divide the items into different categories and analyze the data pertaining to these specific categories.

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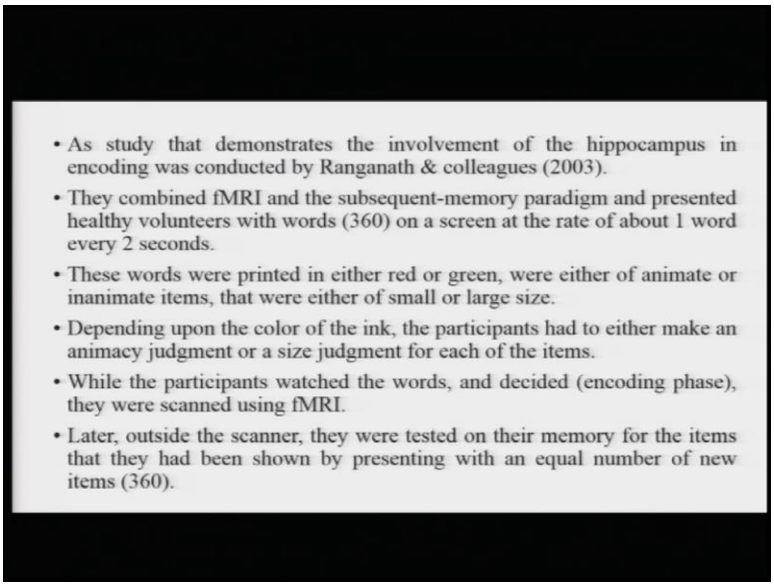

Now, one study that demonstrates the involvement of hippocampus in encoding was conducted by Ranganath & colleagues in 2003. They combined the fMRI and the subsequent memory paradigm and presented healthy volunteers with around 360 words on a screen at the rate of about 1 word every 2 seconds. These words were printed in either red colour or green colour and could be either inanimate or animate items. Say for example if I am talking about pictures of animals those will be inanimate, if I am talking about pictures of furniture items then those will

be inanimate and this could be either in red ink or green ink or you know in small size or large size.

Say for example a chair is generally small but a cupboard is a large size thing. Rat is generally small but elephant is a large size animal. So, you can either basically the participants are asked that depending upon the colour of the ink they had to make a judgement of either animacy whether this thing is animate or inanimate or size. Whether it is a small object or big object.

So, this is basically their task. Now, while the participants were watching these words and deciding basically learning these things, grasping these things which is referred to the encoding phase they were being scanned using the fMRI. Later outside the scanner they were tested on their memory for the items they had shown by presenting an equal number, memory for items that they had been shown by presenting the old items with an equal number of new items.

So, now in the final list they have shown around 720 items basically which means 360 old and 360 new items.

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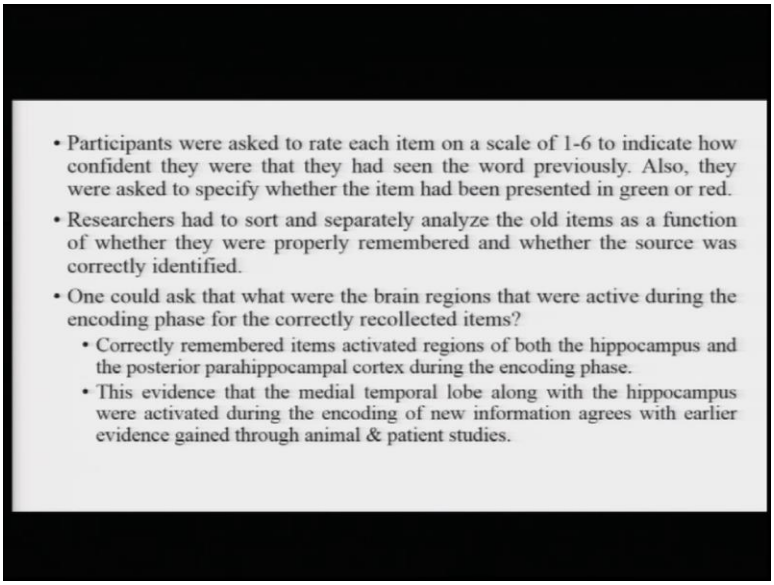

Now, participants were asked to rate each item on a rate of 1 to 6 to indicate how confident they were that they had seen these words previously. Also they were asked to specify whether the item had been presented in green or red. So, basically it will work as a sort of source memory

kind of analysis that not only you have to tell that you have seen this before you have to exactly tell how did you see it and what context etcetera.

Now, researchers as I said had sorted and separately analyzed the old items as a function of whether they were properly remembered or whether the source was correctly identified. So, you can basically say there could be items that were properly remembered but the source was not identified and some items which were remembered correctly as well as the source was also correctly identified.

So, you can kind of sort these items into these categories and then look at the data. Now, one could ask that whether that what were these brain regions that were active during the encoding phase for the correctly recollected items? Now, the correctly remembered items activated of regions of both the hippocampus and the posterior parahippocampal cortex during the encoding phase. So, these are the two regions which were activated and they are very very important. Let us say for the encoding of new information.

Now, this evidence that the medial temporal lobe along with the hippocampus is getting activated during the encoding of new information agrees with some of the earlier evidence that we have talked about through animal and patient studies. So, we know now that the hippocampus is region of the brain that is involved in case of encoding new information.

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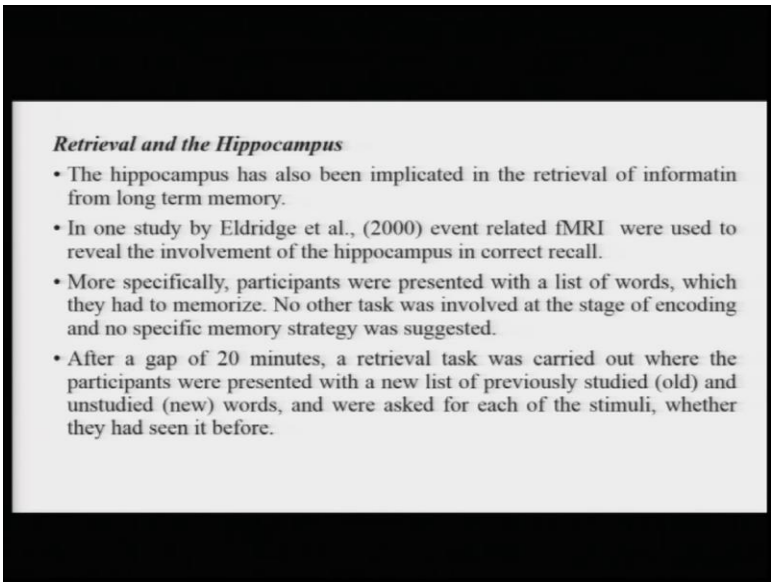

Let us look at retrieval now. Now, the hippocampus has also been implicated in the retrieval of information from long term memory. In one of the studies conducted by Eldridge and colleagues in 2000 they used event related fMRI to reveal the involvement of hippocampus in correct recall. More specifically what they did was they presented the participants with a list of words they had to memorize and there was no other task no other memory strategy was suggested.

So, basically you just given a list of words and you have to memorize that. After a gap of 20 minutes, a retrieval task was carried out where the participants were presented with a list of previously studied and some unstudied so old items and some new items and they were basically asked the simple questions that whether they have seen the words before or not. So, that is basically the simple setup.

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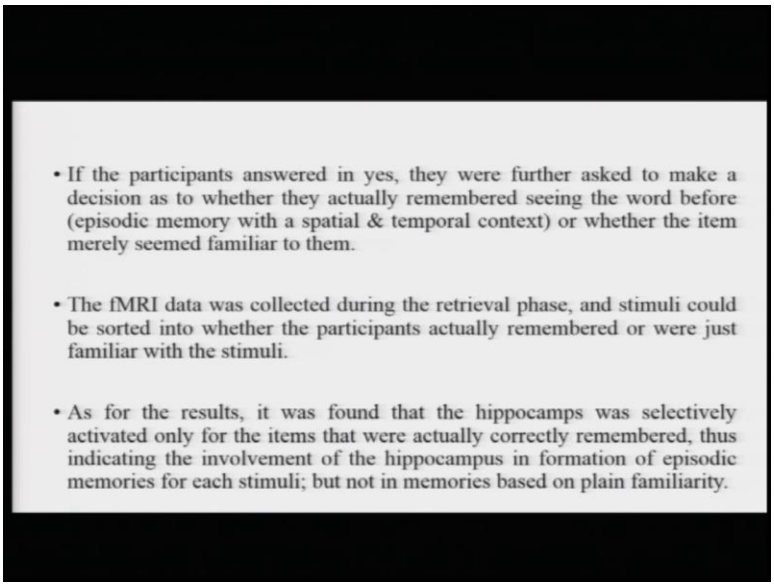

Now if the participants answered in yes, they were further asked to make a decision as to whether they actually remembered seeing this particular word in the previous list or they were just familiar with the item. Something that I was telling you before. Now, the fMRI data was collected now during the retrieval phase.

Remember we are now focused at figuring out retrieval you know activation of the brain during the retrieval phase. So, the fMRI data was now collected during the retrieval phase and the stimuli can be sorted into whether the participants actually remembered or were just familiar with these items.

So, what happened with respect to the results? It was found that the hippocampus was selectively activated only for the items that were correctly remembered, thus indicating the involvement of the hippocampus during correct recall or during the formation of episodic memory for each stimuli but not when say for example people are answering just by the virtue of familiarity.

So, this is a very important distinction. We will talk about this in a bit more but the idea is that the hippocampus is being activated when the participants are correctly remembered the information which is basically the entire episode of seeing that word in the list and with its entire context. Instead of just being plainly familiar with this I am saying okay I might have seen this earlier.

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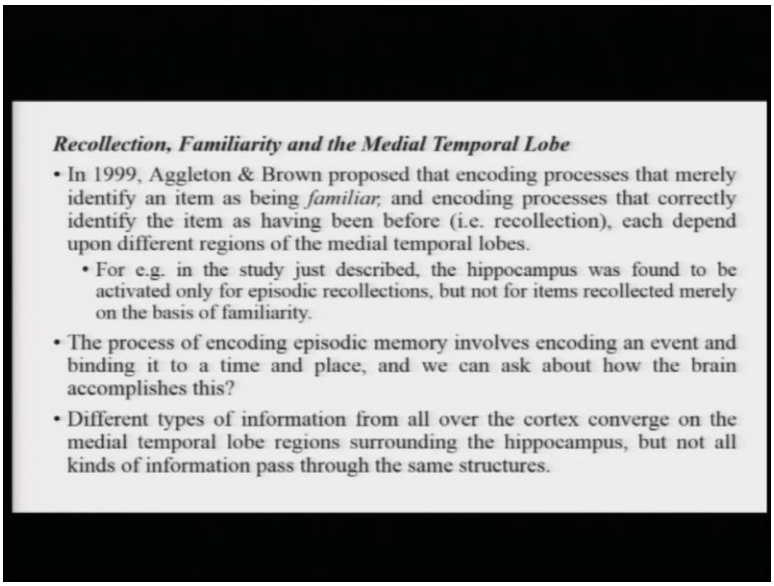

Now, let us make this distinction between correct recollection as in the earlier study and familiarity. It seems that once you are talking about somebody actually recollecting the word from a list or say for example actually recollecting a particular episode or an event, you are actually talking about an entire sequence of information that is episodic in nature and it is encoded along with the context.

On the other hand familiarity is just that okay I know this word, I am not very sure that where have I encountered it did I actually encountered it in your test list. So, these two are slightly different processes and let us now see what basically is the contribution of the medial temporal lobe system including the hippocampus, the parahippocampus etcetera in these two different kinds of processes.

So, in 1999 Aggleton and Brown proposed that the encoding processes that merely identifies an item as being familiar and the encoding process that correctly identifies the item as being seen before depend upon different regions of medial temporal lobe. So, this is the proposal. The process of encoding episodic memory involves encoding an event and binding it to a time and place.

Say for example you might come across somebody going let us say you are out shopping in a mall or somewhere you come across a person and you remember that okay I have met you at this conference at this place in this venue. This is basically recollection of that entire episode of

encountering this person or you could just say that oh I think I remember you, I think I know you but I can not really recall where from and how do I remember you. So, these are the two different processes. Remember that in recollecting properly you are including the time and place information as well. What are the brain areas that help you to do this?

Different types of information from all over the cortex converges on the medial temporal lobe regions surrounding and these regions are surrounding the hippocampus but not all kinds of information pass through the same structures. It could be that all though the all of the information is converging at the medial temporal lobes there is bit of divergence as to where this information is flowing further to.

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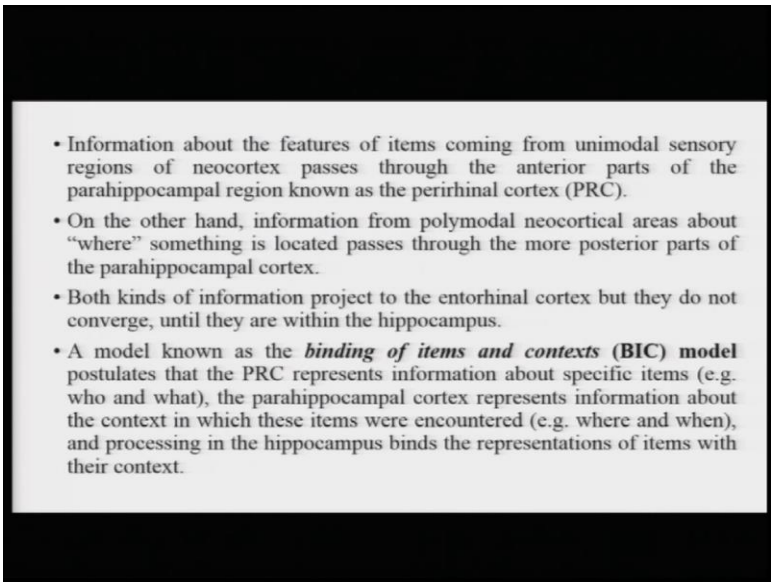

Information about the features of items coming from unimodal sensory regions of the neocortex that is the cerebral cortex passes through the interior parts of the parahippocampal region known as the perirhinal cortex. Its the anterior, it's the further part of the parahippocampal region which is your perirhinal cortex.

On the other hand, information from polymodal neocortical areas basically about where something is located passes through the slightly more posterior parts of the parahippocampal cortex. So, you can see that there is a distinction between where these two informations are being processed. Both kinds of information project finally to the entorhinal cortex but they do not

really converge or join together until they are within the hippocampus. So, they do not converge within the hippocampus. They sort of get out of the hippocampus and then maybe.

Now, a model known as the binding of items and contexts model the BIC model basically the perirhinal cortex represents information about specific items about who and what and the parahippocampal cortex represents information about the context in which these were encountered so where and when and processing in the hippocampus basically puts these two informations together. It binds the representations of items with their contexts. So, let us see.

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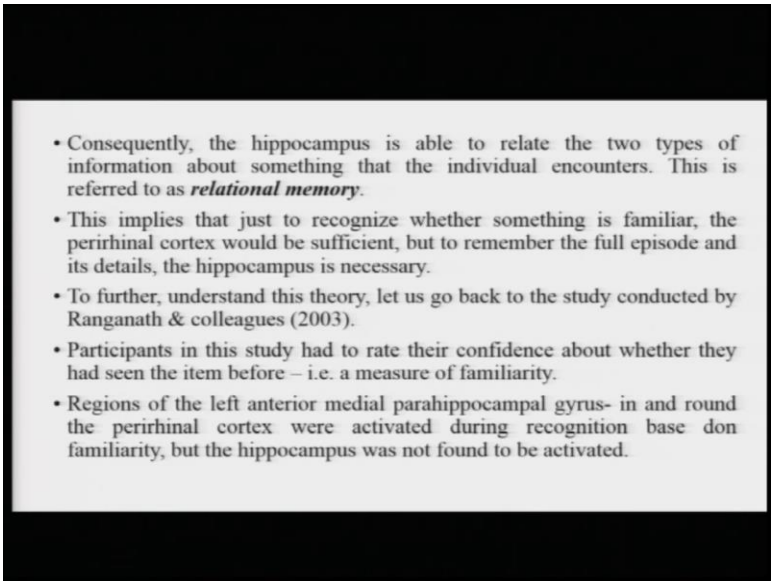

Now, consequently what the hippocampus is able to do is that it is able to relate the two types of information what and where about something that the individual encounters and this is basically referred to as relational memory. When you can basically recall some of the facts related to all of these things.

Now, this basically implies that just to recognize whether something is familiar, the perirhinal cortex would be sufficient basically just the what information is going to be sufficient. But to remember the full episode you need the hippocampus because the hippocampus is the one that will bind this what information with the where and when informations. Now, to further understand this theory let us go back to the study which was conducted by Ranganath and colleagues 2003 we have just talked about it.

Now, participants in this study had to rate their confidence about whether they had seen these items before. This conference level thing is more like a measure of familiarity. Now, regions of the left anterior medial parahippocampal gyrus in and around the perirhinal cortex were activated during the recognition based on familiarity but the hippocampus was not found to be activated. So, in just familiar cases you see that the hippocampus is not really required but the anterior medial parahippocampal gyrus which is basically your perirhinal cortex is being implicated.

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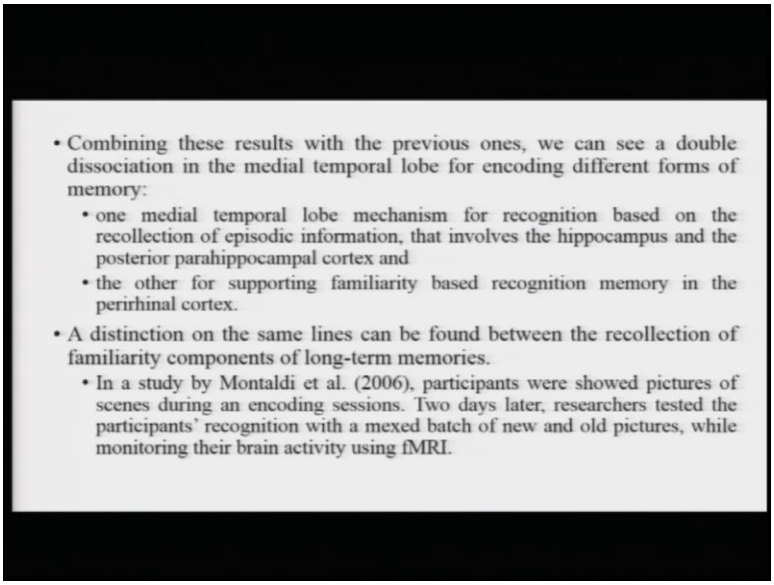

Now, combining these results with the ones that we previously know we can see that there is almost double dissociation in the medial temporal lobe for encoding different forms of memory. One medial temporal lobe mechanism is responsible for recognition based in recollection of episodic information that involves the hippocampus and the posterior parahippocampal cortex and the other mechanism is basically there for supporting familiarity based recognition memory which is your anterior areas and the perirhinal cortex. Now, a distinction on the same line can be found based on the recollection of familiarity components of long-term memories.

There was a study done by Montaldi and colleagues in 2006 where participants were showed pictures of scenes during encoding session. There were shown pictures of several different kind of scenes and 2 dyas later researchers were to test the participant's recognition memory with mixed batch of old and new pictures while and when this test was going on that is where their brain activity was being monitored using fMRI.

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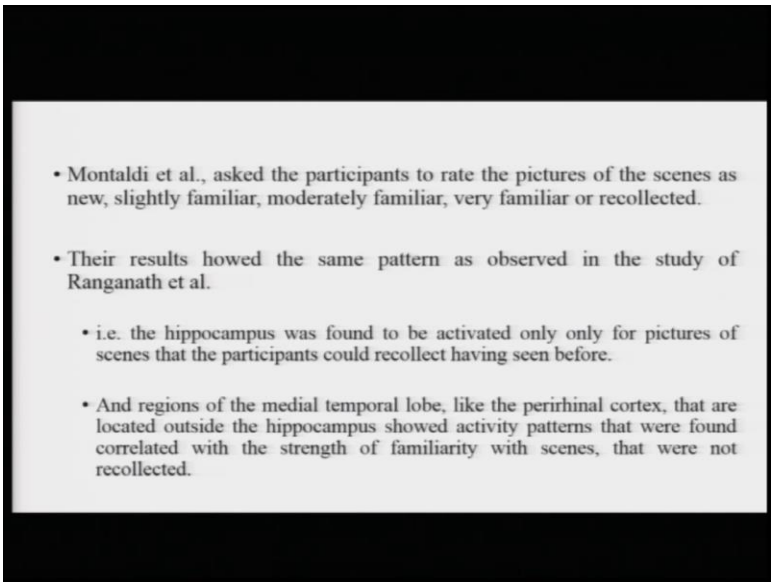

Now, Montaldi and colleagues asked the participants to rate the pictures of the scene as new, slightly familiar, moderately familiar, very familiar or recollected. So, for which you have the context information as well. Now, the result showed the same pattern as observed in the study of Ranganath and colleagues that is the hippocampus was found to be activated only for pictures that were recollected as having been seen before and regions of medial temporal lobe like the perirhinal cortex that were located outside the hippocampus showed activity patterns that were found correlated with the strength of familiarity.

So, from slightly familiar to moderately familiar to very familiar the strength of this activation in these areas were correlated with this strength of familiarity.

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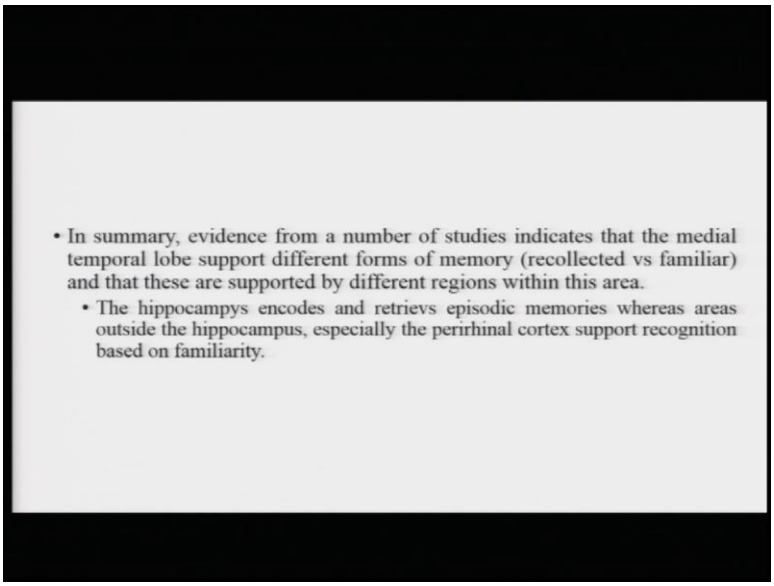

Now, in summary we can basically put all of these things together and we can say that evidence from a number of studies indicates that the medial temporal lobe support different forms of memory that is either recollected versus familiar and that these are supported by different regions within this temporal lobe area. So, more precisely the hippocampus encodes and retrieves episodic information episodic memories whereas areas outside the hippocampus especially the anterior parts the perirhinal cortex supports recognition based on familiarity. So, this is something that I am sure you should remember. Now let us talk about relational memory.

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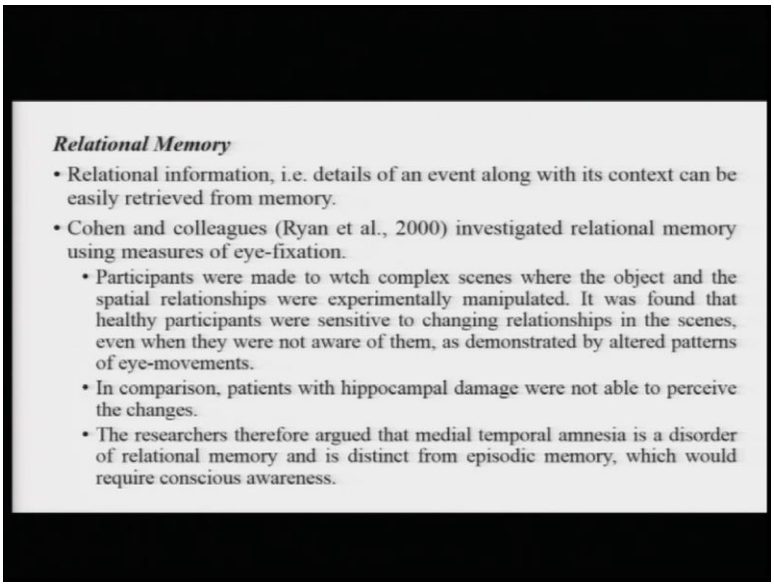

Now, relational information basically refers to the details of an event along with its context and this can be easily retrieved from a memory. Cohen and colleagues investigated relational memory using measures of eye fixation. So, in their study participants were made to watch complex scenes where the object and the special relationships were experimentally manipulated.

It was found that the healthy participants were sensitive to changing relationship between this objects and the special relationships within the scenes even when they were not aware of them as demonstrated by their eye movement patterns. In comparison, patients who had hippocampal damage were not really able to perceive the changes within these things.

The researchers therefore argued that medial temporal lobe and amnesia is a disorder of relational memory and it is slightly distinct from episodic memory, which would basically require conscious awareness. So, the proposal is episodic memory requires conscious awareness and relational memory may or may not require conscious awareness and hence these two are slightly different things.

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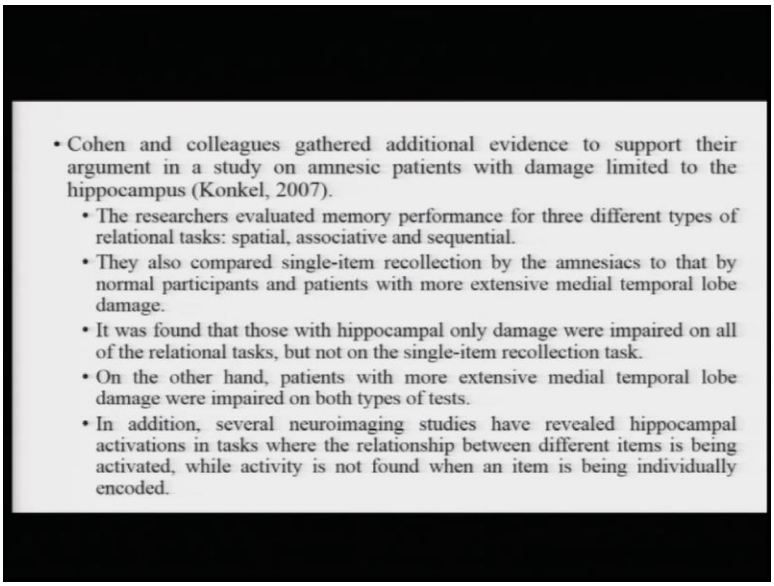

Now, Cohen and colleagues also gathered additional evidence to support their argument in a study based on amnesic patients. So, these amnesic patients had limited damage to the hippocampus. The researchers evaluated their memory performance for three different types of relational tasks spatial relations, associative relation and sequential relation.

They also compared the single item recollections by the amnesiacs to that by normal participants and patients with more extensive medial temporal lobe damage. So, there are three types of patients amnesiacs, normal participants and patients which have extensive damage to their medial temporal lobe.

Three kinds of relationship. Spatial relationship x is to the right or the left of y, associative relationship x is associated with y. Say for example fountain pen those kind of things. Sequential relationship, this comes after this. So, three kinds of relationships, three kinds of patients. Now, it was found that those people with hippocampal only damage were impaired upon all three of these association or relational task but not with a single item recollection task. So, when you have to remember just a single item without the relational information without the context information people with hippocampal damage also perform that all right.

But as soon as we have to have any kind of relational information and hippocampus is damaged you will not be able to recollect that information. Now, on the other hand patients with more extensive medial temporal lobe damage were impaired upon both types of test. In addition

several neuroimaging studies have also revealed that hippocampus activations are found in the task where the relationship between different items is being activated while activity is not found when an item is being individually encoded. So, something that is very consistent with what we are discussing just now.

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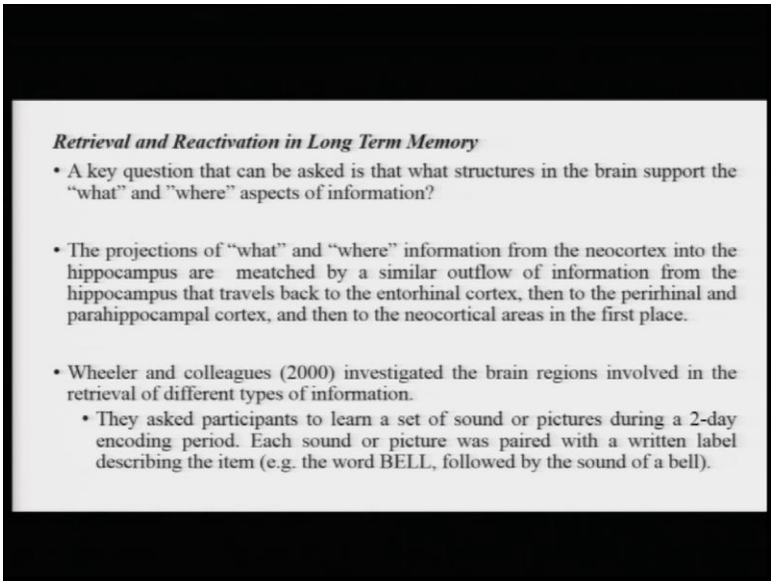

Now, let us talk a little bit about the process of retrieval and reactivation in Long Term memory. Now, a key question about these things can be asked is what are the structures of the brain that support the what and where aspects of information? The projections of what and where information from the neocortex into the hippocampus are actually matched by a similar outflow of information from the hippocampus that travels back to the entorhinal cortex, then to the perirhinal cortex, parahippocampal cortex and then to the neocortical areas in the first place. So, this is a sort of a loop, this is sort of a network.

Now, Wheeler and colleagues in the year 2000 investigated the brain regions that are involved in retrieving different types of informations. They asked participants to learn a set of sounds or pictures during a 2 day encoding period. So, a set of sound or a set of pictures were to be learned. Each sound or picture was paired with the label a word that would label him. Say for example the sound of the word bell is associated with the actual word bell written there. So, in that way.

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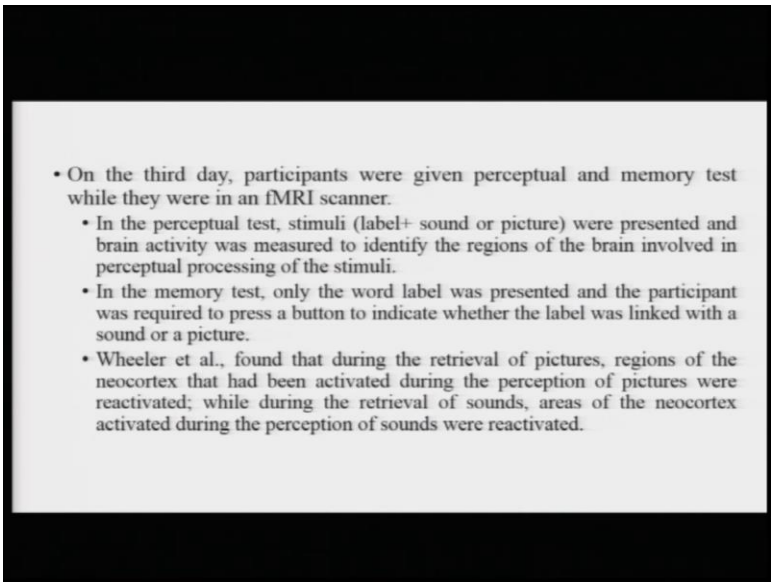

Now, on the third day, participants were given perceptual and memory test while they were in an fMRI scanner. In the perceptual test, stimuli that is the label plus the sound or picture were presented and brain activity was measured to identify the regions of the brain involved in the perceptual processing of the stimuli.

In the memory test, only the word label was presented and the participant was asked to press the button to indicate whether this label was associated with a sound or a picture. So, you have to recall it and then you will be able to press that okay this label came with a picture, this label came with a sound.

Now, Wheeler and colleagues found that during the retrieval of pictures the regions of the neocortex that had been activated during the perception of pictures were reactivated. Similarly during the retrieval of sound the regions that had been initially activated during the perception of sounds were reactivated. So, the same regions that are involved in a initial perception of processing of these stimuli are actually getting activated or a subset of these regions are getting activated when you are retrieving this information.

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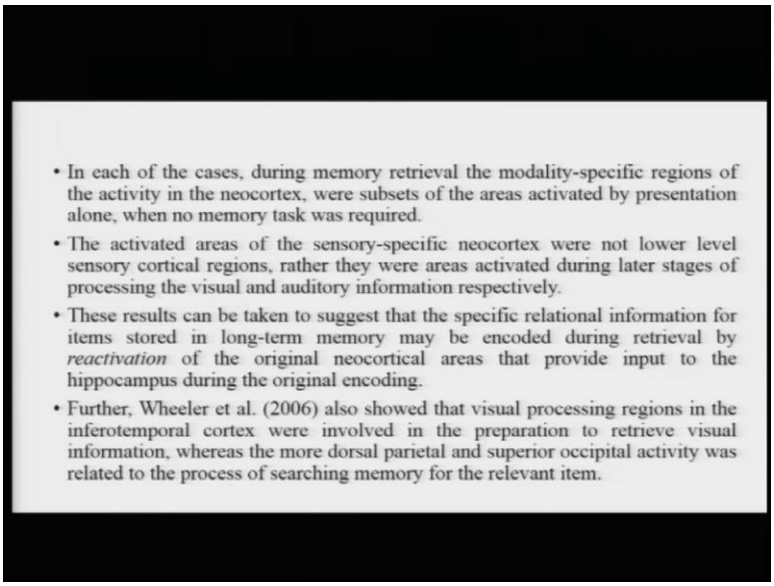

In each of these cases during memory retrieval the modality specific regions of the activity in neocortex were subsets of areas activated by the presentation alone when no memory task was required. So, this is basically what idea they said. Now, the activated areas of the sensory specific neocortex were not the lower level early visual area 17 18 area but they were actually areas that are involved in later stage processing.

High level processing of this stimuli. If you look at these results, these results can be taken to justify that specific relational information for the items stored in long term memory may be actually encoded during retrieval by the reactivation of the original neocortical areas that provide input to the hippocampus during the original encoding.

So, what happens is basically what I am trying to say is when you are encountered with the stimulus you do the initial perceptual processing and then if you recall that the same areas which were involved in a perceptual processing will get reactivated. Now, this reactivation basically will leads to you know the encoding or say for example this reactivation will basically lead to the instantiation of this relational information.

Now, further Wheeler and colleagues in the year 2000 also showed that visual processing regions in the inferotemporal cortex were involved in the preparation to retrieve visual information. So, visual processing region are also been involved when you are planning to remember, when you

are planning to recall certain visual information whereas the more dorsal parietal and superior occipital activity was related to the process of searching the memory for an item.

So, it seems that while you are trying to retrieve information or say for example there are two things. One is that modality specific areas are getting activated, two is the same areas that are involved in earlier perceptual processing of these items if you even encountered them before will prepare the recall or will get activated while you are retrieving that information. So, this is something very interesting about this whole process of recall.

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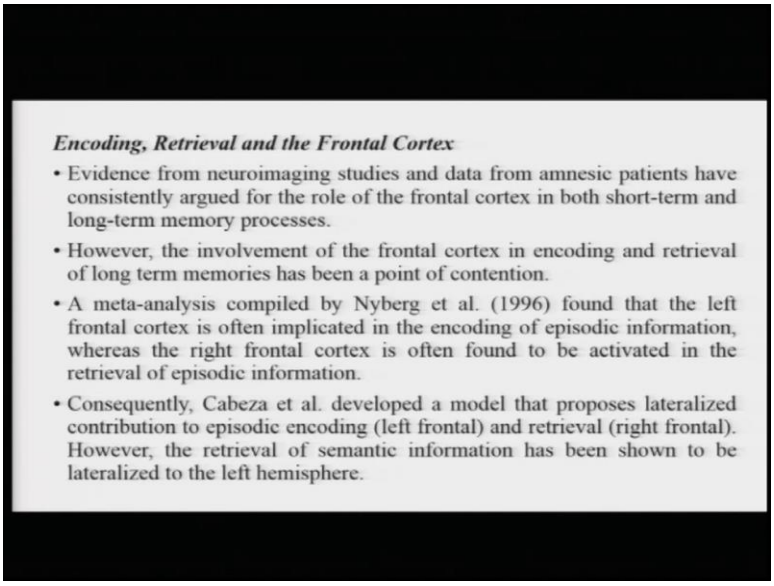

Now, let us look at we have talked about the medial temporal lobe enough. Let us talk little bit about the role of the frontal cortex. Now evidence from several neuroimaging studies and data from amnesic patients have consistently argued for the role of the frontal cortex in both short term and long term memory processes.

However, the involvement or the nature of the involvement of the frontal cortex in encoding and retrieval has not really been very very clear. A meta analysis compiled by Nyberg and colleagues in 1996 found that the left frontal cortex can be implicated in the encoding of episodic information, whereas the right frontal cortex can be found to be activated while you are retrieving the episodic information. So, there is a degree of lateralization here.

Consequently Cabeza and colleagues actually developed a model that proposed that lateralized contribution to episodic encoding from the left frontal and retrieving from the right frontal areas. However, the retrieval of semantic information is not found to be lateralize in this manner. The retrieval of semantic information has mostly shown to be lateralized to the left hemisphere. So, this is typically what we know about the contribution of the frontal lobes.

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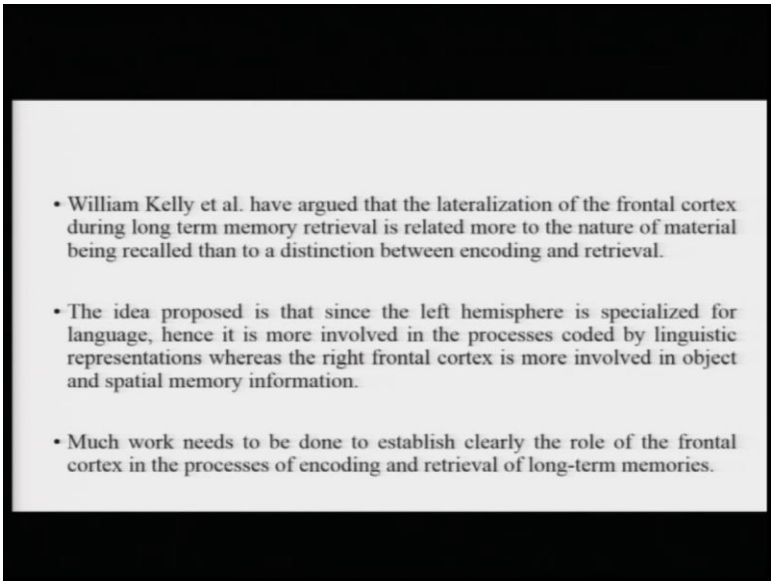

Now, another proposition comes from William Kelly and colleagues who have argued that the lateralization of the frontal cortex during long term memory retrieval is related more to the nature of the material that is being recalled. What they say typically us that since the left hemisphere is specialized for language and linguistics processing when you are recalling material encoding through linguistics representation that is why the left hemisphere will get activated.

Similarly the right frontal cortex will be involved more in object and spatial memory information. So, for example when you are talking about object features and spatial memory kind of features. Now, still it is not very clear and we are not going to discuss this in much detail, the only thing we can say here at this this point that there is a lot of work that needs to be done in this area to establish clearly the role and the nature of the frontal cortex involvement in the processes of encoding and retrieval of long term memories.

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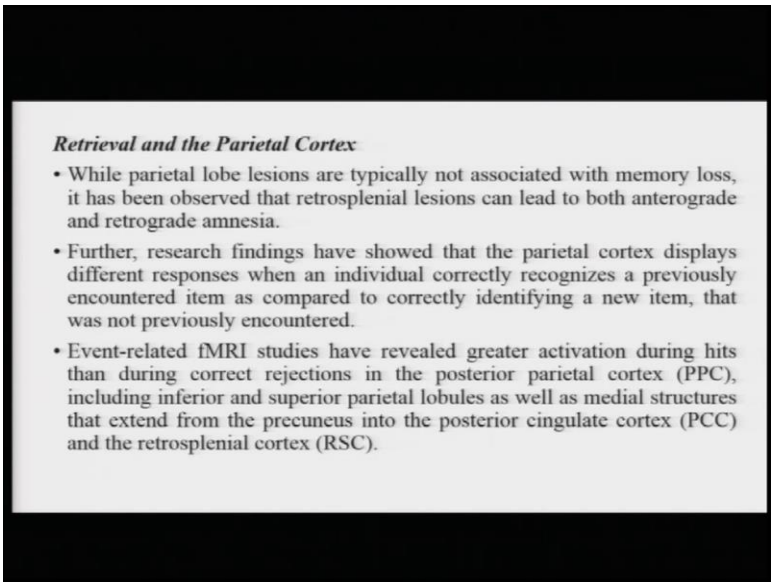

Now, let us finally talk about the parietal cortex. Now, parietal lobe lesions are not associated with memory loss but it has been observed that retrosplenial lesions can lead to both anterograde and retrograde amnesia. Further, research findings have also shown that the parietal cortex displays different responses when an individual correctly recognizes a previously encountered item as compared to identifying a new item. So, when there is a degree of memory involvement, there is a difference of response that you can see emanating from the parietal cortex.

Now, event related fMRI studies have revealed greater activation during hits than during correct rejections in the posterior parietal cortex that is the PPC including the inferior and superior parietal lobules as well as the medial structures at the cortex that extend from the precuneus into the posterior cingulate cortex that is the PCC and the retrosplenial cortex that is the RSC. So, this is the nature of activations that is observed that sort of can implicate or link the role of parietal cortex in the memory processes.

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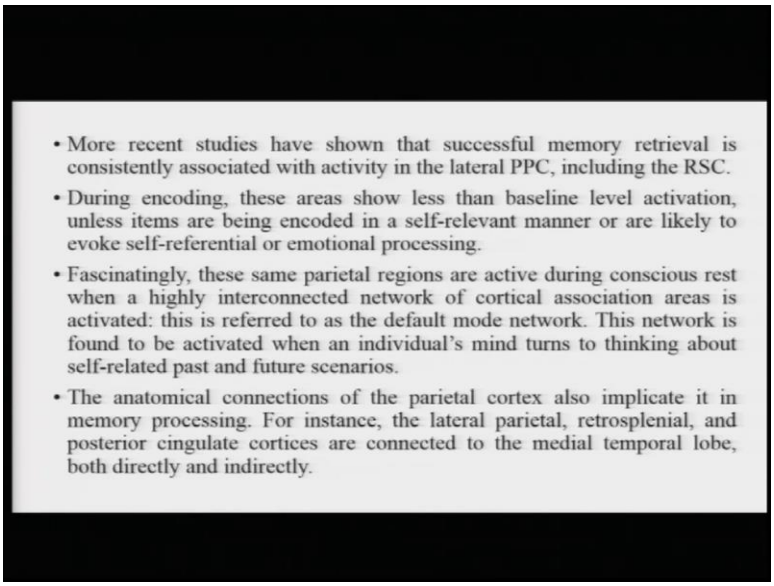

Now, more recent studies have shown that successful memory retrieval is consistently associated with activity in the lateral posterior parietal cortex including the retrosplenial cortex. So, there is some association with respect to retrieval or recall with the parietal cortex. Now, what happens during encoding? During encoding, these areas show less than baseline level activation unless items are being encoded in a self relevant manner.

Say for example I can show you a picture of 5 objects, two of these objects are owned by you and then I ask you in a memory test which of these objects presented have you seen before. The objects that you know you recognised as being your own you will when you recall them you have basically encoded them in relation to you this is my bag, this is pencil box something like that.

So, unless you are encoding stuff in relation to yourself as being your own or as being related to you in some manner then you know these activations are sort of not seen. So, PPC and RSC activations are not seen at the encoding phase unless you sort of encode item in relation to yourself.

Fascinatingly these are the same parietal regions that become active during conscious rest when a highly interconnected network of cortical association areas is activated. So, when you are trying to relax when you are trying to rest this is referred to as the default mode network. The default mode network is a fascinating network of the brain and there is lot of research about it.

Now, this network is found to be activated when an individual's mind turns to thinking about self related past and future scenarios. Now, the anatomical connections lets talk about the connection of the parietal cortex. The anatomical connection of the parietal cortex also implicate it in memory processing. For instance, the lateral parietal, retrosplenial and the posterior cingulate cortices are connected to the medial temporal lobe both directly and indirectly. So, they do have projections in the parietal lobe.

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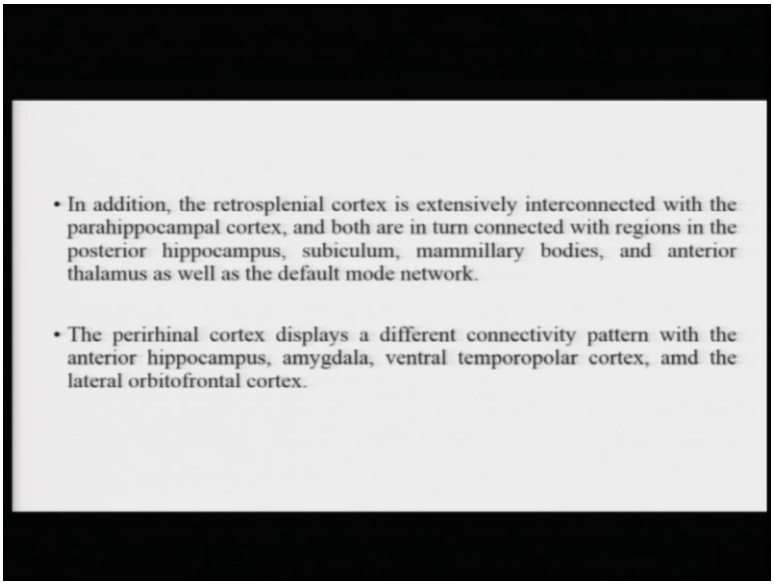

In addition, the retrosplenial cortex is extensively interconnected with the parahippocampal cortex and both are in turn connected with regions in the posterior hippocampus, subiculum, mammillary bodies and the anterior thalamus as well as the default mode network. So, this connection is basically with all the regions that are involved in memory processing and that sort of already tells you that there is no way that the parietal cortex or these regions from the parietal cortex are not involved in some kind of memory processing.

Now, the perirhinal cortex displays a slightly different connectivity pattern because its connected with the anterior hippocampus, the amygdala, the ventral temporoporal cortex VTPC and the lateral orbit of the frontal cortex, the lateral OFC.

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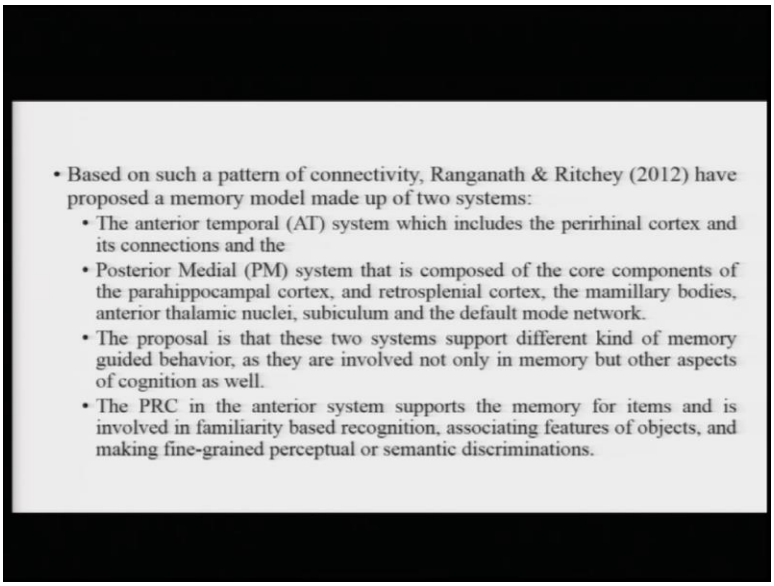

Now, based on this kind of pattern of connectivity, Ranganath and Ritchey in 2012 have proposed a memory model that is made up of two kinds of systems. There is one which is called the anterior temporal system which includes the perirhinal cortex and its connections and there is the another one which is the posterior medial or the PM system that is composed of the core components of the parahippocampal cortex, the retrosplenial cortex the mammillary bodies, anterior thalamic nuclei, subiculum and the default mode network.

Now, the proposal they are Ranganath and Ritchey put forward is that these two systems support two different kinds of memory guided behaviour and they not only involved in memory processing but also in other aspects of recognition. Say for example say that the PRC in the anterior system basically which is the perirhinal cortex and the anterior system supports the memory for items and is involved in familiarity based recognition.

Now, remember this is something which we are already talking about in the studies of Ranganath and colleagues earlier. So, the PRC and the anterior system probably supports the memory for items and is involved in familiarity based recognition associating the features of objects and making fine grained perceptual or semantic discriminations.

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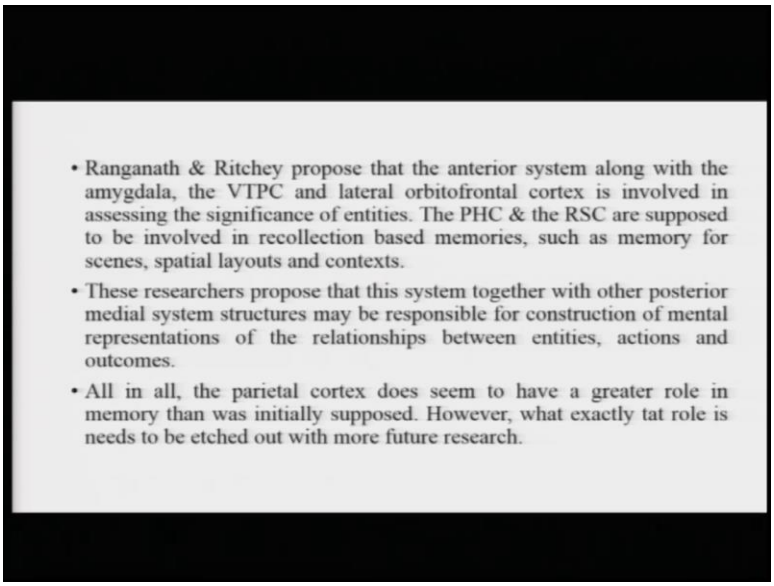

Ranganath and Ritchey further proposed that the anterior system along with the amygdala, the VTPC and the lateral OFC is involved in the assessing the significance of entities. How significant they are, are they related to myself, do they have any threat value those kind of things. The parahippocampal cortex and retrosplenial cortex are supposed to be involved in recollection based memories basically when we have to remember the relational information as well such as memory for scenes, special layouts and contexts.

Now, these researchers propose that this system together with other posterior medial system structures may be responsible for construction of mental representations and of the relationship between the entities actions and outcomes. So, this is not really just memory but slightly more higher order cognitive processes. All in all the parietal cortex does seem to have a very very important role in memory than was initially supposed. However, what exactly that role is needs to be better etched out with more and more future research. Thank you.