Memory
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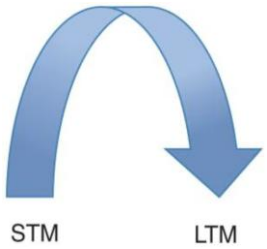
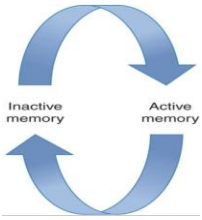
Lecture - 39
Memory Reconsolidation – I

Hello, I welcome you all to the lecture series on memory. Today, we are going to start a new topic: memory reconsolidation. The topic of memory reconsolidation has recently gained a lot of attention in memory research. This topic has gained a lot of attention for two reasons: memory, once consolidated, undergoes changes upon retrieval. At this labile stage, it can be consolidated with some new information.

The reason why memory undergoes reconsolidation at this labile state is that we can maintain and update it with new information. This is a routine procedure for memory to maintain itself over time, and occasionally, we add new information to the old. Hence, the consolidation becomes labile again. At this stage, you can update it, which after updating undergoes reconsolidation. Memory does not always need to be updated, but upon retrieval, it becomes labile and active.

As the state passes, it gets consolidated. Before we delve into a detailed discussion on memory reconsolidation, let us explore some aspects and ideas about memory. As we have discussed earlier, memory is depicted as going through several phases. These phases, discussed in the previous lecture, include the acquisition stage, encoding stage, retention, storage, and retrieval. The encoding stage ensures information is acquired and ready to be consolidated.





Source: Nader K. (2015). Reconsolidation and the Dynamic Nature of Memory. *Cold Spring Harbor perspectives in biology*, *7*(10), a021782. https://doi.org/10.1101/cshperspect.a021782

Stabilization phase ensures that now the information which has been acquired should be stabilized. So a synaptic consolidation is required. In this synaptic consolidation, the two synapses, three synapses, four synapses collectively coming together ensures that the information to be encoded and stored. Once the encoding and stabilization phase is over, then the maintenance phase starts. This maintenance phase ensures that the information which has been stored or saved now should be maintained over a period of time.

And once that information is being encoded, stabilized and maintained over a period of time, it can be retrieved easily. Maintenance phase for the maintenance, it is important that the information should be retrieved. based on reactivation. So, when we talk about the short-term memory information going to long-term memory information, one such factor is the sleep factor. If people are not having enough sleep, the information may not transfer.

And that is what we have seen in the case of people who are having the problem of insomnia where the long-term memory information encoding seems to be disrupted. stabilization is not there and if the information is not there then you cannot maintain that information at all or if the information has reached also in some way to your LTM but in a very crude form, distorted form then also you cannot maintain it. For the maintenance it is important that the information should be reaching it in an unimpaired or undistorted form. Finally, once you have stored it, then at the time of retrieval, it should be there.

So, when we talk about such thing, long term memory upon retrieval leads to LTL, long term memory retrieval. But it is very important for us to understand that whatever we are referring as the retrieval after sleep, when the memory is moving from encoding to storage to retrieval phase, not all memories undergo maintenance or update. This is an important part. And not all memory, not only undergo maintenance or update, but consolidation also.

Not all information what you acquire undergo consolidation this we have discussed in previous lecture that the coordination between frontal cortex and hippocampus this coordination this exchange between the two brain regions at the time of sleep deep sleep during the rapid eye movement stage the slow wave spindle is generated and this ensures this triggers the information which has been acquired and which is present there in your hippocampus to travel back or move back to the frontal cortex and this back and forth projection from hippocampus to frontal cortex get structured and coordinated and after this coordination the information passed down into our long-term memory so not all

memory undergo maintenance and update or consolidation this because if not all memories undergoing into consolidation then there are certain boundary conditions of memories there. These boundary conditions ensure that the memory in one form or the other has certain limitation. And these limitations, because of these limitations, sometimes memory is robust in nature and sometimes memory is labile in nature, sometimes memory is distorted in nature. Because of these boundary conditions,

The memory can have different forms, and these things ensure that the condition should be met. So robust in nature, narrow in nature, or distorted. Now, as we are discussing memory, acquisition and memory stabilization were considered as active states. And when consolidation has occurred, when the information has been stored, that state of memory is called an inactive state. Because the information is not actively involved.

There is no action involved; the neurons are in a very stabilized state. At that state, this state, at this state, memory is consolidated. Now, this consolidated memory, if you are retrieving it, if there is retrieval, or you are doing reactivation using a cue, then this inactive memory becomes active memory, and once it is active, then upon update, it undergoes reconsolidation. This is the reconsolidation.

Again, the consolidation process, again the storage is happening. Was the active memory there? Now you have three possibilities. You update it. You leave it as it is.

When you are updating it with some new information, then the consolidated memory, this inactive memory will be a revised inactive memory. New inactive memory will be there. New consolidated memory will be there. If you are not doing anything, then the same impression will be left. So two possibilities there, one is the update has happened or update has happened, same impression.

So what we talk about is that the maintenance of memory is portrayed as the active process. that consolidated long-term memory can become susceptible to disruption and restoration upon reactivation. So once you have reactivated the memory, once you have done the retrieval, this memory which is active in this state is labile in nature. At the state of labileness, the memory is very So this is state of labile upon retrieval.

This is very sensitive. And this sensitive memory is not prone to disruption. It is likely to get disrupted. Along with disruption, restoration is also there. Which means you can update it.

And this entire process is called as reconsolidation. So once the long term memory can become susceptible to disruption and restoration upon reactivation, a process is termed as reconsolidation. Because this memory upon reactivation is going to get consolidated again. It is an important part here. From inactive to active memory state or active to inactive state, the memory process is time dependent and protein synthesis dependent.

Upon reactivation, you have a very small window up to 6 hours to modify it, to modify the memory, to update the memory. More than 6 hours, update may not happen. But it is important for us to also understand not all memory, not all types of memory can undergo re-convalidation. So you cannot update every memory. Some memories are very robust in nature and do not require an update.

They are okay. If we keep on updating the memory, then execution of simple tasks such as brushing the teeth, brushing your teeth, eating your meal can become ambiguous and complex in nature. So memory process is time dependent and protein synthesis is time dependent as such 6 hours. Protein synthesis is once the reactivation is occurring, memory is active state, you apply the protein blocker at this stage, you will block the memory. Now it is an important aspect for us to understand that how

this consolidation memory is giving strength. Now very important part here we have to understand that the initial theory on memory suggested that any information which we are encoding and leading to storage this consolidation this storage or consolidation is on stone. You cannot erase it. You cannot update it. But five decades of research in this area suggested that this is stored memory upon retrieval with a cue or reactivation with a cue makes this

Consolidated memory, labile again, labile in nature. And this labile nature, now you can do an update. And it goes reconsolidation. Now the point is that this reconsolidation process is not unique to human beings. It is also there and has been found in different species such as nematode, fish, rats, etc.

And it also suggests that memory undergoes reconsolidation to be strengthened. This reconsolidation is happening to maintain the memory. The maintenance, why maintenance is required? A house which you have built in 1970, if you need that the house should exist next 100 years, then you from time to time you need to restore the house. Restoration practice is important.

From time to time you have to protect the house and in such case You need to maintain the house. How do you maintain the house? With whitewashing, plastering, changing, adding various chemicals against various species such as termite, against sunlight, rain, protection against these disasters or these increase the longevity of the house. Similarly, if we want to store a memory for long period of time, we have to maintain it.

And not only we have to maintain it, but we have to update it from time to time. So if we were in the school, we were taught that apple is red in color. But as we grew up, We come to know that apple can be green in color. And this is what we updated the information about the apple color.

In addition to that, the taste of the apple can be updated as well. Now, what we understand is that the consolidation process is trying to strengthen the information or memory. recently acquired memory will be consolidated within a time window of six hours. For the rest of the memories lifetime the memory will engage in reconsolidation mechanism. What does it indicate?

It indicates that the first time the memory is undergoing consolidation it requires six hours. Once the memory is being consolidated Then only the update or maintainers is required. This update and maintainers is the going to engage the reconsolidation mechanism. Now, when such aspects of memory is there, consolidation and reconsolidation, then one thing is very clear.

that the consolidation and reconsolidation are sharing similar mechanism. However, because reconsolidation is also involved in the maintenance and update of memory, they have distinct mechanism also. Now they are similar and distinct. When we talk about the similar mechanism, we have to also mention here that the mechanisms are not identical in nature. This means reconsolidation may be same as consolidation.

upon reactivation consolidated memory is becoming soft again and moving towards the consolidation this consolidated upon reactivation after the update moving to consolidation may share similar mechanism but also has distinct mechanism and the mechanism cannot be identical in nature even if they are similar Recent studies in human fMRI study has revealed that the consolidation of fear memory involves the amygdala but reconsolidation activates the frontal cortex. So if we understand clearly with this cartoon, the new information which we have encoded

The new information that is very unstable in nature. This is in active state. Once the memory has moved to stored after encoding, it has moved to storage stage. This stored memory is stable or in active state. This inactive state which we discussed earlier, upon reactivation, reactivation with what?

The retrieval or the relevant reminder. This reminder is nothing but it is a cue. So if a relevant cue is given, this makes the inactive state memory to active state again. That is unstable. Once it has become unstable, it will undergo reconsolidation again.

And at this reconsolidation state, you have an opportunity of window where you can modify the memory. How can you modify the memory? By behavioral means. Studies have shown exposure therapy You induce stress.

How? Clear stress task. This stressor is going to interfere with the reconsolidation process. The moment it interferes with the reconsolidation process, the memory will be altered, degraded or strengthened or updated. Only three possibilities are there.

Whenever we treat the memory, whenever we treat the memory, electrical stimulation, electrical or magnetic stimulation, pharmacological method, CBT method, etc. What we have seen, only three possibilities there. Either you will enhance the memory, either you will dampen the memory, or you will leave as it is. Only three possibilities there.

Once you treat the memory with different agent, electrical magnetic stimulation, pharmacological method, CBT etc. so here stressor women pharmacological agent drug administration earlier we have discussed about the benzodiazepines that creates amnesia if that drug is given here the memory will not only be altered But it will be completely blocked, leaving definitely some impression. NIPS, non-invasive brain stimulation.

Okay. But not all memories undergo modification. Not all memories can be treated, and after the treatment, they can be modified. Some memories do not undergo modification, updating, or reconsolidation. These boundary conditions of memory are under experimental parameters.

When researchers have done their studies in the lab, they have found the age of the memory. If the memory is very old, it will take time for retrieval. If the age of the memory is very old, then it may be independent; it may have been independent of the memory structures. It may have become independent of memory structures. As a result, it becomes very difficult, first, to target the memory; secondly, the retrieval itself might be a very challenging task.

So, the retrieval and reactivation with the cue become a challenging task because the age of the memory is very old. Training strength matters if you have trained a lot to acquire and encode any information. This training makes the memory more robust in nature. And when it makes the memory more robust in nature, this type of memory cannot undergo reconsolidation. Because the strength is so great. In contrast, if the training strength is very low,

It is something which you have spent only seconds remembering. The strength is very weak. As a result, this memory can undergo reconciliation easily. When learning reaches an asymptote, when learning reaches saturation, when learning reaches saturation, Then memory update cannot be done either.

The stimulus is significantly shorter or longer. So if you are presenting the stimulus—sorry, the duration of the reactivation stimulus—is significantly shorter or longer. What does this mean? When the retrieval is there—retrieval with a cue or reactivation with a cue—it is important for us to understand what the duration of this cue is. The duration of the cue can be short, or it can be long. If the duration of the cue is short, then it will be a trigger. If the cue is short, then it is a trigger, and it will reactivate the memory. However, when the cue is

longer, it acts as an extension. Extension process—what does this mean? It means that it gives the participant satisfaction that a bad instrument is not going to appear. This discussion we are having is with respect to the fear conditioning model. So, if the reactivation duration is short, then it is only going to activate the fear in the participant.

But if the duration is a little long, then it acts as an extension trial. Reactivation can occur in new environments. And when reactivation occurs in a new environment, it seems to be effective. And sometimes it has been observed that reactivation occurring in a new environment does not trigger the memory as well. Now it is very important for us to understand that reactivation is seamless and predictable.

And this predictability ensures memory undergoes reconsolidation. What is the function of reconsolidation? The function of reconsolidation is that older or stronger memories are not destabilized by reactivation. So, these memories are not destabilized upon reactivation. So, reconsolidation may be a lingering consolidation process.

So, if the destabilization has not occurred, This means a lingering consolidation process has been there. The consolidation process is there just normally. Reconsolidation cannot update it. Responses learned over time gradually strengthen.

As the responses are there, the participant learns that for extremely bad experiences, I do not have to press a key. For the good experience or pleasant feeling, I have to press the key. As the participant learns from the responses, these responses, as time passes by and as the trial progresses, become more and more strengthened. Synaptic re-entry. When we talk about synaptic re-entry and reinforcement, it means that the synapse

upon reconsolidation is updating and maintaining the synaptic connection. This synaptic connection is getting updated or maintained repeatedly every time the memory is retrieved or reactivated. This reinforcement ensures the synapse re-enters again and again. Reactivation during awake experience. may induce processes that facilitate the modification of associations.

So the association of the network seems to be modified upon reactivation. Previously experienced stimuli extract biologically significant predictors. So whenever we retrieve information, this retrieval facilitates the modification of those associations. And then we update the information with some new details every time we check the photographs of our dear ones.

Now, reconsolidation function stems from the fact that strongly encoded memory at learning asymptote can still be made labile. by exposure to novel, unexpected or long reactivation stimuli. What does this mean? Something which we have learned can and encoded it strongly can undergo reconsolidation upon long reactivation. Now, as we discussed earlier, long reactivation leading towards extinction or if you are bringing some novelty into it.

This novelty or this unexpected nature can also help in the memory update. Newly learned items can intrude into the old knowledge if existing memories are first retrieved. So the newly learned items are actually getting association with the new information. Memory may be maintained in a permanently modifiable form. that permits the updating of each trace when relevant information is encountered.

Every time when an individual is encountering an important information, memory is undergoing inactive state, active state. Under the relevant information, this inactive state to active state modifies the memory. Partial or complete destabilization of memory. Can

we do a partial destabilization or complete destabilization? This destabilization means uncertainty.

Uncertainty: how different memories of similar stimuli can be integrated and retrieved. Different forms of memories exist. And the uncertainty is how this information can be combined together. How this information can be combined together. Reactivation of memory may destabilize a trace.

Why does it destabilize a trace? Upon reactivation, the memory, which was inactive, becomes active again. And this active state of memory is time-dependent and protein synthesis-dependent. And that is why this trace is destabilized. Any interference or amnesic treatment upon reactivation of memory may lead to amnesia.

In modifying the memory, the new impression may block this labile portion, but the other parts remain intact. Some parts can be updated. Some parts remain intact, as you can see here. This we don't have to update; this we have to update. Under certain conditions, it might be expected that the non-labile portion of the memory could mediate the expression of the behavior. What does it mean? It means that if the memory is undergoing reconsolidation, then the behavior which is unchanged.

This portion which is not non-labelized, this didn't become labile. Then this remain as it is and the area which is being labilized undergo update and the area which is non-labelized is resulting into the expression of the behaviour or this is the root cause of the behaviour. This is not being changed. It remains, this behaviour remains as it is. Memory malleability and memory reconsolidation.

Memory malleability is nothing but memory, labile nature, memory soft nature. Loftus did a study demonstrated misinformation effect and it suggested that how new information will be included in the existing memory representation because it becomes plastic after reactivation. Upon reactivation, long term memory upon reactivation become long term memory retrieval. And this long-term memory retrieval which we are calling is plastic in nature, labile in nature, soft in nature, malleable in nature. Inside bias, phenomena that causes people to overestimate their ability to predict events.

So long term memory into retrieval leads to association of related memories. So this long term memory retrieval is leading towards the related memories that are biased towards the supplementary information suggesting the reconsolidation hypothesis. As we discussed about the misleading post-event information, misinformation fact, hindsight

bias, people overestimating the ability to predict event. The third is targeting and reconsolidation. Memory reconsolidation process mediate the targeting effects.

How is it mediating the targeting effects? The interference effect is a function of memory modification how the memory can be updated interfering something is going to block or inhibit the memory function and once the blockage or inhibition happens there is an update and there is a modification initiated by retrieval of existing memory in presence of new information. The suggestion that reconsolidation process underpines these distortions.

What we are talking about? When we are moving from active state, sorry inactive state to active state we are using the process of reactivation this reactivation when we are using this active memory is becoming inactive and upon reactivation once this inactive to uh inactive to active is happening happening memory is after reactivation is followed by And when reconsolidation is happening, it is distorting this. Distortion is there.

Why distortion? Because reconsolidation is adding information. Defining the characteristics of memory reconsolidation is Post-reactivation short-term memory, but intact post-reactivation short-term memory. After the reactivation, the short-term memory is intact.

Its expression is there, intact. But in long-term memory, if we talk about inactive to active, impairment occurs post-reactivation in long-term memory. So this part may be intact, and this part is getting impaired. Post-reactivation long-term memory—sorry, after this impairment occurs. The important aspect we have to understand is what reconsolidation is doing.

Reconsolidation is distorting this process. As a result, the information is getting forgotten. So, what did we study in this lecture? We studied the memory process—how the consolidation of memory requires encoding, stabilization, maintenance, and retrieval. This consolidated memory is moving from an active state to an inactive state.

Once it has reached the inactive state from the active state, updates or modifications cannot be made. But recent literature suggests that upon retrieval and reactivation with the relevant cue, it can become active again. Once this memory becomes active again, it is malleable, labile, and soft in nature. In this state, you can distort, modify, or update memory. Why does memory undergo reconsolidation?

It undergoes reconsolidation because memory requires an update and memory requires a maintenance. And because of this maintenance and update, we are able to hold on to information from our childhood to adulthood. We do remember of our past, of our school time, of our dear ones and then once we have retrieved that information, we update that information where they are now, what are they doing currently and then consolidate it. This is a normal process for memory and that is why reconsolidation is an important aspect of memory.

Once the memory is consolidated, It only requires an update and maintenance. But not all memories can undergo reconsolidation. That is why the boundary conditions of memory come. And this boundary condition of memory talking about the age of memory.

If the age of memory is, the memory age is very old, then it cannot undergo reactivation. One or two studies have shown that if the age of memory is very old, old memories can also undergo reconsolidation upon long retrieval trial. Strength of memory, when the training is too much, it makes the memory so robust in nature that the well-trained memory can also do not undergo reconsolidation. Then also the retrieval and the duration of retrieval is important. Now the retrieval, if it is presented for short duration, it can make the memory from inactive to active state.

But if the duration of the queue or retrieval is long, then it will start acting or behaving as an extinction trial. We even studied the functions of reconsolidation. Why is reconsolidation required under different circumstances, under various circumstances? The relevance of reconsolidation: some studies suggest that it distorts the stabilized memory. Why does it distort the stabilized memory?

Because we are updating it and maintaining it with some new information. The entire process of consolidation and reconsolidation is a protein synthesis and time-dependent process. This reconsolidation process has been found across species. Even we have to understand that the consolidation and reconsolidation processes are distant from each other, yet they may have some similar mechanisms. But they can never have an identical mechanism.

Some neurotransmitter studies have also suggested that the upregulation and downregulation of various neurotransmitters assist in the process of reconsolidation. With this, I end this session here, and in the next lecture, we are going to talk about some more updates on memory literature. Thank you.