

Memory consolidation and reconsolidation: drug addiction



**ASSIGN
BUSTER**

Memory Consolidation and Reconsolidation: Implications for Drug Addiction

- Jayan Samarakoon

Abstract

This paper looks at the current knowledge and debate surrounding memory reconsolidation. After a brief overview of consolidation and reconsolidation including the associated theories of each process the paper delved into the literature surrounding reconsolidation and critically evaluated research articles which either reinforced or shed doubt onto the physiological mechanisms of reconsolidation. The paper then discussed possible applications of this knowledge in the treatment of drug addiction, in particular the efficacy of blocking NMDA receptors to disrupt reconsolidation. Guidelines for future research concerning human trials were outlined.

Memory Consolidation and Reconsolidation: Implications for Drug Addiction

Memories affect human behaviour (Nader & Einarsson, 2010). An understanding of how memories are formed would give insight into the mechanisms that underlie behaviour. This paper will look at the physiological processes that affect memories such as consolidation and reconsolidation in particular the current knowledge and debate surrounding these memory processes. The paper will then delve into how this knowledge could affect psychology, in particular the realm of drug addiction. This will be done by critically evaluating the current literature and outlining areas for future research.

Memories are believed to be located in the synapses between neurons of the brain (Nader & Einarsson, 2010). New memories change the strength of the synapse which results in an adjustment of the specific memory (Clopath, 2012). Memory is categorised into two forms, short-term and long-term memory. The difference between the two is a process called consolidation which affects information stored in long-term memory via strengthening the neuron pathways affected by the memory called the memory trace (Nader & Einarsson, 2010). Consolidation is the process of stabilizing a memory trace after the initial behavioural experience (Dubnau & Chiang, 2013). Many different studies have found that several types of interference such as inhibiting protein synthesis, disrupting the function of specific proteins, and brain lesions or trauma can disrupt the process of consolidation (Alberini, 2011). These studies have formed the basis of understanding the different consolidation models. Consolidation consists of two distinct processes, synaptic consolidation and system consolidation (Clopath, 2012). Synaptic consolidation involves repeated stimulation of a neuron called long-term potentiation, which results in stable changes at the synapse over time while systems consolidation is a process where memories that are dependant of the hippocampus become independent and move to a separate brain region. Synapses can vary in strength, which is referred to as plasticity (Clopath, 2012). A change in synaptic plasticity can be a short-term change which lasts a few minutes to a long-term change which can last up to a life-time. A long-term change in plasticity is the basic definition of synaptic consolidation. This process allows memory to be consolidation within a single synapse, which cannot be altered by any new memories (Clopath, 2012).

Synaptic consolidation usually occurs within the first few minutes to hours after the memory encoding has happened (Dudai, 2004).

The physiological conditions that cause synaptic consolidation involve many different processes which result in a physical change of the synapse (Dubnau & Chiang, 2013). They include modification and reorganisation of the synapse protein including the membrane receptors. Intracellular signalling proteins such as cAMP and MAPK are recruited to activate cellular remodelling and growth during synaptic consolidation (Dudai, 2004).

The standard model of system consolidation posits that memory is dependent on the location of the encoding in the mediotemporal lobe (Dubnau & Chiang, 2013). Initial memories are formed in the hippocampus via synaptic consolidation and then over a period of weeks or more the memory trace reorganises so that the retention is maintained by the neocortex and is not dependent on the hippocampus anymore (Dudai, 2004). There are some criticisms with this model of systems consolidation. For starters only declarative memory is processed by the hippocampus and as such this model cannot apply to non-declarative memory. An alternative view is called multiple trace theory. Multiple trace theory proposes that the hippocampus region is always involved in the retention and retrieval of episodic memories and that semantic memory follows the standard model of system consolidation (Dubnau & Chiang, 2013).

These models of consolidation assume that the process of consolidation occurs just once. This assumption is currently undergoing some criticism and debate on whether it is valid or not. Research has shown that the retrieval of

a memory trace can induce a phase where the memory is malleable to change (Tronson & Taylor, 2007). One paper proposed that memory was a dynamic process with two different states, an active state where memories both new and reactivated are labile to change and an inactive state where the memories stabilise over time (Nader & Einarsson, 2010). Memory reconsolidation is induced by the reactivation of a specific memory (Reichert & Lee, 2013). This reactivation process causes the memory trace to become destabilised into a 'labile' state, a state where the memory pathway can be changed. The process to return the destabilised memory into a stable form is called reconsolidation and is dependent on protein synthesis (Reichert & Lee, 2013). Destabilisation occurs when L-type voltage-gated calcium channels and cannabinoid CB1 receptors are activated, along with synaptic protein degradation in the dorsal hippocampus (Reichert & Lee, 2013).

A study examined if it was possible to reactivate a consolidated memory into a labile state and introduce new information (Forcato, Rodríguez, Pedreira, & Maldonado, 2010). Participants were asked to learn an association between five cue-syllables and their respective response-syllables. 24 hours later the memory was reactivated and the subjects were given additional information, in this case three extra syllable pairs. The participants were tested on their knowledge the third day. The results showed that the new information was successfully incorporated into the former memory since both sets of syllables were successfully retained in memory when the instruction stated to add the new information to the old memory, unlike the condition where the instruction was omitted. This condition showed evidence that the two sets of information were encoded independently from each other due to

interference in retrieval. The study used a verbal reminder (briefly mentioned the previous pairs) to try and trigger reconsolidation. They did not assess if retrieval of the memory actually occurred. One method of bypassing the requirement of assessing if memory retrieval occurred is to design an experiment where the process of memory reconsolidation is interrupted, which should impair memory retrieval at a later date. A study conducted in 2010 successfully demonstrated that if the reactivation of a memory is followed by an emotionally aversive stimulus results in impairment when recalled at a later date (Strange, Kroes, Fan, & Dolan, 2010). This study gives evidence that memories can be impaired following their retrieval.

Reconsolidation has been found to occur not just in humans but in other animals as well (Robinson & Franklin, 2010). A Considerable amount of research exists which indicates that when an animal is reminded of a previously learned experience the memory of that experience undergoes reconsolidation. This is supported by findings which show that treatment with a protein synthesis inhibitor immediately after re-exposing the experience can produce amnesia of the memory itself, due to the fact that recalling a memory triggers reconsolidation which requires the production of new proteins (Cai, Pearce, Chen, & Glanzman, 2012). One study looked at how the amnestic drugs propranolol and midazolam would affect reconsolidation in rats (Robinson & Franklin, 2010). They did this by exposing the rats to a box which contained both morphine and a saline solution in separate areas. The rats were exposed to this apparatus either four or eight times depending on the experimental condition. Afterwards the rats received either no dosage, or an injection of an amnestic drug. The rats were retested

two and seven days after the dosage in the four pairings condition and with the eight pairings condition they were tested eight times in 48 hour blocks. The result showed that the amnestic drugs disrupted reconsolidation for weak memories (four pairings condition) and had little effect for strong memories (eight pairings condition).

A study conducted by Cammarota, et al. (2009), examined if reconsolidation would occur in an inhibitory avoidance task using rats. The rats were trained in an inhibitory avoidance task and 24 hours later were exposed to the task again. After the exposure the rats were injected with a protein synthesis inhibitor and tested on the avoidance task for the third time. The results revealed that the protein synthesis inhibitor had no effect on memory retention. If reconsolidation had occurred there would have been a change in memory retention. This study used a short time period to measure reconsolidation.

In the study conducted by Robinson & Franklin (2010), there was evidence that reconsolidation had occurred yet in the study by Cammarota, et al. (2009), there was no evidence of memory reconsolidation occurring. There are two major differences between the two studies which may shed light into the discrepancy regarding the results. The study which showed reconsolidation used many repeated exposures to the memory stimulus and measured the possible effects of reconsolidation over a period of two weeks (Robinson & Franklin, 2010), unlike the other study which only had two training sessions (as opposed to four or eight) and tested for any reconsolidation effects within 24 hours of the last training session

(Cammarota, Bevilaqua, Medina, & Izquierdo, 2009). These findings show <https://assignbuster.com/memory-consolidation-and-reconsolidation-drug-addiction/>

evidence that memory reconsolidation may only occur in specific instances, with the two studies giving evidence that training strength and time may be two factors which affect reconsolidation. Research into finding the prerequisites of reconsolidation would be beneficial.

One study looked at the limitations or boundaries of memory reconsolidation (Wang, De Oliveira Alvares, & Nader, 2009). In the study Wang, et al. (2009) looked at the effects of strong training on fear-associated memory and reconsolidation. The data suggested that when 10 pairings were used instead of one the memory did not undergo reconsolidation until after thirty days have passed. By looking at the molecular mechanisms the researchers found that certain NMDA receptor subunits have to be stimulated in the BLA during reactivation of the memory to begin reconsolidation. They found that strong training could inhibit the activation of the NR2B receptor subunit which resulted in the fear stimulus not triggering reconsolidation. These results suggest that even though reconsolidation exists there are certain prerequisites that have to be met to start the process, such as the strength of the training and the time that has elapsed since encoding. These limitations may be the reason why some studies have not found a reconsolidation effect.

These research articles show that reconsolidation is an actual process of memory. Reconsolidation can be the mechanism which enables our memories to be modified or updated since the memory that undergoes the process is activated often in situations which present additional complementary information (Lee, 2009). Since old, well-established memories can undergo reconsolidation there exists the possibility to exploit <https://assignbuster.com/memory-consolidation-and-reconsolidation-drug-addiction/>

the destabilisation of the memory and either disrupt or even erase it completely (Milton & Everitt, 2010). Therefore reconsolidation could be seen as an adaptive technique which can potentially affect or guide future behaviour. This has many potential applications. Many psychiatric disorders are due to underlying aberrant memories, such as drug addiction (Milton & Everitt, 2010). Drug addiction is a chronic and relapsing disorder whereby the main risk of relapse comes from the presentation of environmental cues which have been previously associated with harmful drug use (Font & Cunningham, 2012). These cues are memories which can possibly be targeted and changed by memory reconsolidation to influence future behaviour.

One study looked at reconsolidation and alcohol dependence in mice (Font & Cunningham, 2012). The mice were trained with either a strong or weak conditioning process. The animals were then given an injection of propranolol, a receptor antagonist and tested for memory consolidation a day later. The test found that memory retention was not affected by the antagonist. The study examined the effects of propranolol after the reactivation of the memory therefore the antagonist was introduced after reconsolidation had started. A study that looks at the effects of an antagonist that has been introduced before reconsolidation has started may yield different results.

One study looked at drug-associated memories and their relationship with amygdala NMDA receptors (Milton, Lee, Butler, Gardner, & Everitt, 2009). They hypothesised that NMDA receptors in particular glutamate receptors within the amygdala are crucial for the consolidation between environmental

<https://assignbuster.com/memory-consolidation-and-reconsolidation-drug-addiction/>

conditioned stimuli and the effects of addictive drugs, therefore the NMDA receptors must be crucial for the reconsolidation of drug-associated memories (Milton, et al., 2009). The study used a behavioural task that measures the conditioned reinforcing properties of a drug-paired stimulus by first exposing the stimulus, then injecting a NMDA receptor antagonist before a memory reactivation session. They found that the antagonist disrupted drug-associated memory and decreased the conditioned reinforcement effect. This effect lasted four weeks which was the length of the experiment. Although there was a link found when the receptor antagonist was injected before the reactivation session there was no difference when the drug was introduced after the session which indicates that the receptor may only have a limited role in reconsolidation. These results suggest that controlling the glutamate levels at the NMDA receptor may be useful in preventing relapses although further research has to be done, particularly on the actual effect of NDMA receptors on reconsolidation and the length this effect lasts for.

In summary the current knowledge of reconsolidation is quite sufficient to have an impact in psychological applications such as treating drug addiction. Knowledge about the specific physiological mechanisms of reconsolidation from animal studies is a good foundation to advance towards human experiments. Further research into the specific physiological mechanisms which underlie reconsolidation would help create effective treatment plans as would moving from animal studies to human trials.

References

Alberini, C. M. (2011). The role of reconsolidation and the dynamic process of long-term memory formation and storage. *Frontiers in behavioral neuroscience, 5*, 12. doi: 10.3389/fnbeh.2011.00012

Cai, D., Pearce, K., Chen, S., & Glanzman, David L. (2012). Reconsolidation of long-term memory in *Aplysia*. *Current Biology, 22* (19), 1783-1788. doi: 10.1016/j.cub.2012.07.038

Cammarota, M., Bevilaqua, L. R. M., Medina, J. H., & Izquierdo, I. (2009). Retrieval does not induce reconsolidation of inhibitory avoidance memory. *Learning & Memory, 11* (5), 572-578. doi: 10.1101/lm.76804

Clopath, C. (2012). Synaptic consolidation: an approach to long-term learning. *Cognitive Neurodynamics, 6* (3), 251-257. doi: 10.1007/s11571-011-9177-6

Dubnau, J., & Chiang, A.-S. (2013). Systems memory consolidation in *Drosophila*. *Current Opinion in Neurobiology, 23* (1), 84-91. doi: 10.1016/j.conb.2012.09.006

Dudai, Y. (2004). The neurobiology of consolidations, or, how stable is the engram? *Annual Review of Psychology, 55* (1), 51-86. doi: 10.1146/annurev.psych.55.090902.142050

Font, L., & Cunningham, C. L. (2012). Post-retrieval propranolol treatment does not modulate reconsolidation or extinction of ethanol-induced

conditioned place preference. *Pharmacology, Biochemistry and Behavior*, *101* (2), 222-230. doi: 10. 1016/j. pbb. 2012. 01. 009

Forcato, C., Rodríguez, M. L. C., Pedreira, M. E., & Maldonado, H. (2010). Reconsolidation in humans opens up declarative memory to the entrance of new information. *Neurobiology of Learning and Memory*, *93* (1), 77-84. doi: 10. 1016/j. nlm. 2009. 08. 006

Lee, J. L. C. (2009). Reconsolidation: maintaining memory relevance. *Trends in Neurosciences*, *32* (8), 413-420. doi: 10. 1016/j. tins. 2009. 05. 002

Milton, A. L., & Everitt, B. J. (2010). The psychological and neurochemical mechanisms of drug memory reconsolidation: implications for the treatment of addiction. *The European journal of neuroscience*, *31* (12), 2308. doi: 10. 1111/j. 1460-9568. 2010. 07249. x

Milton, A. L., Lee, J. L., Butler, V. J., Gardner, R., & Everitt, B. J. (2009). Intra-amygdala and systemic antagonism of NMDA receptors prevents the reconsolidation of drug-associated memory and impairs subsequently both novel and previously acquired drug-seeking behaviors. *The Journal of Neuroscience*, *28* (33), 8230-8237. doi: 10. 1523/JNEUROSCI. 1723-08. 2008

Nader, K., & Einarsson, E. Ö. (2010). Memory reconsolidation: an update. *Annals of the New York Academy of Sciences*, *1191* (1), 27-41. doi: 10. 1111/j. 1749-6632. 2010. 05443. x

Reichelt, A. C., & Lee, J. L. C. (2013). Memory reconsolidation in aversive and appetitive settings. *Frontiers in behavioral neuroscience*, *7*, 118. doi: 10. 3389/fnbeh. 2013. 00118.
<https://assignbuster.com/memory-consolidation-and-reconsolidation-drug-addiction/>

Robinson, M. J. F., & Franklin, K. B. J. (2010). Reconsolidation of a morphine place preference: Impact of the strength and age of memory on disruption by propranolol and midazolam. *Behavioural Brain Research*, *213* (2), 201-207. doi: 10.1016/j.bbr.2010.04.056

Strange, B. A., Kross, M. C. W., Fan, J. E., & Dolan, R. J. (2010). Emotion causes targeted forgetting of established memories. *Frontiers in behavioral neuroscience*, *4*, 175. doi: 10.3389/fnbeh.2010.00175

Tronson, N. C., & Taylor, J. R. (2007). Molecular mechanisms of memory reconsolidation. *Nature Reviews. Neuroscience*, *8* (4), 262-275. doi: 10.1038/nrn2090

Wang, S.-h., De Oliveira Alvares, L., & Nader, K. (2009). Cellular and systems mechanisms of memory strength as a constraint on auditory fear reconsolidation. *Nature Neuroscience*, *12* (7), 905-912. doi: 10.1038/nn.2350