Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

RECONSOLIDATION-BASED TREATMENTS FOR ANXIETY DISORDERS: CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

Isabella Smith , Institute of Space Research, Moscow State University, Russia

Abstract

At the present, effective treatments are available to reduce anxiety symptoms and their associated distress. Nevertheless, it is frequently observed that anxiety responses are recovered after extinction, without being clear the responsible mechanism of such phenomenon. For decades, it has been presumed the existence of a reconsolidation mechanism. Such mechanism is thought to participate in the re-storage of memories that have been evoked. Recent research apparently reveals that intervention on reconsolidation mechanisms prevents the recovery of anxiety responses that have been previously extinguished. Intervention on these mechanisms could represent an alternative to current psychological treatments for anxiety disorders based on exposure procedures. The objective of the present work is to review the evidence on reconsolidation mechanisms and its effects on the reduction of anxiety responses. Finally some clinical implications will be discussed.

Keywords: reconsolidation; extinction; fear conditioning; anxiety disorders

Introduction

Anxiety disorders (AD) are highly prevalent in the general population (World Health Organization [WHO], 2004). In the National Comorbidity Survey (NCS-R) carried out in the United States (Kessler, Chiu, Dernier, & Walters, 2005),

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

EDs were the most prevalent type of disorders (18.1%). In the work of Labrador, Estupiñá and García-Vera (2010), with a healthcare sample of 856 patients, 31.89% requested help for anxiety disorders. On the other hand, EDs are related to high discomfort and deterioration in the quality of life of those who suffer from them.

Currently, there are effective psychological interventions to address these types of problems (Chambless & Ollendick, 2001; Labrador & Ballesteros, 2011). Techniques such as psychoeducation, exposure, physiological deactivation, cognitive restructuring, problem solving, internal dialogue control techniques or social skills training make up the central core of these Empirically Supported Psychological Treatments (ASD) for anxiety disorders. anxiety.

Various meta-analyses have concluded that ASD have been shown to be effective for different anxiety disorders, both in the field of research and healthcare practice (Hofmann & Smits, 2008; Stewart & Chambless, 2009). It has even been pointed out that they have been shown to be more effective than the treatment usually used in primary care, essentially pharmacological (Roy-Byrne et al., 2010).

Exposure, in its different forms, is considered to be the basic component in ASD for anxiety disorders (Mineka & Zinbarg, 2006). But, although the use of exposure techniques is related to important therapeutic results, including the reduction of symptoms, it has been observed that at least part of the anxiety responses tend to occur again, without the reason for this reappearance being clear (Hermans, Craske, Mineka, & Lovibond, 2006).

Decades ago, it was already pointed out that after evoking or retrieving information from memory, it is necessary to store it again (Misanin, Miller, & Lewis, 1968), calling this process 'reconsolidation mechanism' (Nader, Schafe,

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

& LeDoux, 2000a).). From the moment the information is retrieved from memory until it is stored again (reconsolidated), the contents enter a labile phase and can be altered. In other words, during reconsolidation, the memory trace can be modified (Hupbach, Gomez, Hardt, & Nadel, 2007).

Consequently, this reconsolidation process may have implications in the clinical setting, as it enables an alternative therapeutic approach to the traditional proposal of counterconditioning the anxiety response, typical of techniques such as Systematic Desensitization or Exposure. Taking this reconsolidation process into account, action could be taken by recovering anxiety responses and modifying their content at the time of reconsolidation. Some research aimed at modifying anxiety responses by acting on this mechanism has obtained positive results, indicating that it is possible to prevent the recovery of previously extinguished anxiety responses (Monfils, Cowansage, Klann, & LeDoux, 2009; Schiller et al., 2009). .

The authors of this work considered that the importance of developing new avenues of therapeutic action justifies dedicating efforts to clarify these possibilities. Consequently, the present study aims to review the concepts of consolidation and reconsolidation, as well as the evidence of its role at a neurobiological and behavioral level, to conclude by presenting possible psychotherapeutic implications of intervention on said mechanism.

Consolidation and reconsolidation mechanisms

Consolidation mechanism

Memory consolidation is the process by which recently acquired information moves from storage in short-term memory (susceptible to interference) to permanent storage in long-term memory (Eichenbaum, 2002; Nader et al., 2000a). , less susceptible to interference. This process appears to be gradual,

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

and involves the participation of systems at the molar and molecular levels (Dudai, 1996; Ruiz-Vargas, 2010). Regarding the first, the neural circuits located in medial structures of the temporal lobe seem to be of special relevance. At the molecular level, changes in synapses as a result of learning stand out, particularly the *long-term potentiation mechanism.*(PLP). LTP involves a permanent modification in the response of some cells, accompanied by a structural modification, as a consequence of neural stimulation produced during learning. These structural changes in neurons, which involve the creation of new connections or neural pathways, are supported by protein synthesis that facilitate the development of these new synaptic connections. Once these connections are established, new stimuli will facilitate the appearance of responses, or the same stimuli will facilitate the appearance of new responses. There is evidence that this new learning is consolidated at the molecular level thanks to the PLP mechanism (Eichenbaum, 2002; Kandel, 2001; LeDoux, 1999).

Reconsolidation mechanism

The work of Bartlett (1932) already highlighted that during the retrieval of information the memory trace can be modified. He came to this conclusion by observing that after evoking events from the past, people tend to incorporate information that had not originally been presented, information that may not have been present in said event or directly "invented" information. In later work, with greater experimental control, it was demonstrated that memory traces can be modified, even after being consolidated in long-term memory (Misanin et al., 1968). More recently, Nader, Schafe and LeDoux (2000b) have found that, after reactivating (evoking) memory traces already consolidated in long-term memory, a new protein synthesis is necessary for their

reconsolidation to occur, which highlights an active and "new" process of storage of the recovered memory traces. During this new "re-storage" process, the recovered memory traces can be modified.

Intervention on the reconsolidation mechanism

The evidence that memory traces of long-term memory are modifiable during reconsolidation has sparked interest in procedures aimed at modifying the reconsolidation mechanism (Monfils et al., 2009), considering that therapeutic gains can be obtained in this way. (e.g., preventing retrieval of conditioned responses, changing traumatic memories, etc.).

Interventions to modify the reconsolidation process have been carried out successfully, both through pharmacological and psychological procedures.

a) Modification by drugs: Brunet et al. (2008) worked with a clinical sample of patients with post-traumatic stress disorder (PTSD). The participants were made to evoke the traumatic event (mnemic retrieval), and while one group of them was given a beta blocker (propranolol), the other received a placebo. Given the effect of propranolol in reducing physiological responses associated with anxiety, it was expected that the group to which it had been applied would have difficulty reconsolidating the physiological components of the memory trace. One week later, when the patients were asked to evoke the event again, it was found that the sympathetic activation responses elicited by evoking it were significantly lower in the individuals who received propranolol, compared to those who received the placebo. These results suggest that administering this substance after evoking a traumatic episode may be useful to interfere with reconsolidation processes and reduce physiological responses associated with anxiety. Subsequently, Brunet et al. (2011) extended the previous study by providing propranolol followed by exposure therapy for six sessions. Patients

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

had clinically significant reductions in PTSD symptoms and the gains were maintained throughout six months of follow-up. (2011) extended the previous study by providing propranolol followed by exposure therapy for six sessions. Patients had clinically significant reductions in PTSD symptoms and the gains were maintained throughout six months of follow-up. (2011) extended the previous study by providing propranolol followed by exposure therapy for six sessions. Patients had clinically significant reductions in PTSD symptoms and the gains were maintained throughout six months of follow-up.

b) Modification by psychological procedures: The treatment of TA operating on the reconsolidation mechanism consists of evoking the conditioned stimulus and introducing new information in order to alter the memory trace. The intervention must be carried out during the period in which the contents are stored again and can be modified (period known as reconsolidation window). Monfils et al. (2009), after performing aversive conditioning on rats, proceeded to the extinction phase. A group of individuals was exposed to the conditioned stimulus (evocation) and after an interval between 10 and 60 minutes (the period in which reconsolidation is supposed to occur), extinction was carried out. A second group received the same treatment, except that the interval between evocation and extinction ranged between 6 and 24 hours (period outside the reconsolidation window). A final group was exposed only to the conditioning context. The results indicated that only the group exposed during the reconsolidation window stopped presenting conditioned responses and did not present spontaneous recovery or renewal (e.g., recovery of conditioned response related to the return to the original conditioning context).

Schiller et al. (2009) replicated the work of Monfils et al. in humans. (2009), conditioning a geometric figure with an electric discharge. One day later, one

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

group was exposed to the geometric figure 10 minutes before starting extinction (during the reconsolidation window), a second group was exposed to the figure 6 hours before starting extinction (outside the reconsolidation window).). The third group began extinction without receiving prior exposure to the conditioned stimulus. Twenty-four hours after extinction, the figure was presented again. Only people who received the extinction procedure during the reconsolidation window stopped presenting anxiety responses. The results of the study suggest that the reappearance of conditioned responses can be prevented, if the termination takes place during the reconsolidation window. Finally, Agren et al. (2012) replicated the findings of Schiller et al. (2009), including brain images as a dependent variable. They found that, by intervening on the reconsolidation mechanism, not only is the recovery of conditioned responses prevented, but the memory trace in the amygdala also disappears. In participants who received the extinction procedure outside the reconsolidation window, amygdala activity persisted upon presentation of the conditioned stimulus. By intervening on the reconsolidation mechanism, not only is the recovery of conditioned responses prevented, but the memory trace in the amygdala also disappears. In participants who received the extinction procedure outside the reconsolidation window, amygdala activity persisted upon presentation of the conditioned stimulus. By intervening on the reconsolidation mechanism, not only is the recovery of conditioned responses prevented, but the memory trace in the amygdala also disappears. In participants who received the extinction procedure outside the reconsolidation window, amygdala activity persisted upon presentation of the conditioned stimulus.

Conclusions

Technology Journal of Management , Accounting and Economics (TECH)
ISSN: 2311-3995

Vol. 10 No. 2 (2022)

According to the studies cited in this review, at the behavioral level, the extinction procedure during the reconsolidation window leads to the prevention of recovery of conditioned responses (Monfils et al., 2009). Consistently, at a neurobiological level it has been observed that the administration of protein synthesis inhibitor drugs during the reconsolidation window prevents the recovery of conditioned responses (Nader et al., 2000b). By modifying emotional memory information through intervention on the reconsolidation mechanism, spontaneous recovery is less likely (Monfils et al., 2009).

The results from basic research (Sotres-Bayon, Cain, & LeDoux, 2006; Bouton, 2004) indicate that the mechanism responsible for extinction probably consists of the development of new inhibitory learning (a new connection) and not in the modification of the original connection between the conditioned stimulus and the conditioned response. The permanence of both connections, especially if their strength is close, would explain the spontaneous recovery.

Intervention on the reconsolidation process, instead of promoting new inhibitory learning, would simply modify the memory of existing learning, so that the original stimulus-response connection would be altered. That is, after this intervention the original connection will have been altered and the presence of the conditioned stimulus can no longer provoke the original conditioned response since the stimulus-response connection no longer exists, only the new alternative connection exists. For this reason, from the intervention of the reconsolidation mechanism, phenomena such as renewal and spontaneous recovery would no longer be expected. The advantages of this form of action, at least in theory,

However, the studies described above suggest the need to evaluate interventions on reconsolidation mechanisms in clinical populations. The research carried out

to date (using non-pharmacological means) has been carried out only in analogous populations. Therefore, it is necessary to establish whether interventions targeting the reconsolidation mechanism can benefit in the short and long term for people experiencing clinically significant levels of fear and anxiety.

However, some additional considerations must be made to the intervention on the reconsolidation mechanism:

1. It would be necessary to demonstrate whether this way of acting is really easier, faster or more effective than techniques based on the counterconditioning process.
2. Also, if the results are obtained through really different processes, that is, if in the reconsolidation process changes are really being produced in the neural pathways different from those produced through exposure.
3. Establish the procedure or protocol of action to carry out the intervention on the reconsolidation process (how and when to recover the information, conditions for doing so, how to alter the memory trace, type of information to modify or include...).

In summary, taking into consideration the above, it seems interesting to consider the possibility of acting on the reconsolidation mechanism with the aim of developing new treatment techniques for AT, but it is still in an initial phase and an important development of techniques is needed. research about it.

References

Agren, T., Engman, J., Frick, A., Bjõrkstrand, J., Larsson, E., Furmark, T., & Fredrikson, M. (2012). Disruption of reconsolidation erases a fear memory trace in the human amygdala. *Science*, 337(6101), 1550-1552. [ ]

Bartlett, F. C. (1932). *Remembering: A study in experimental and social psychology.* London: Cambridge University Press. [ ]

Bouton, M. E. (2004). Context and behavioral processes in extinction. *Learning & Memory, 11,* 485-494. doi:10.1101/lm.78804 [ ]

Brunet, A., Orr, S. P., Tremblay, J., Robertson, K., Nader, K., & Pitman, R. K. (2008). Effect of post-retrieval propanolol on psychophysiologic responding during subsequent script-driven traumatic imagery in post-traumatic stress disorder. *Journal of Psychiatric Research,* 42(6), 503-506. [ ]

Brunet, A., Poundja, J., Tremblay, J., Bui, E., Thomas, E. , Orr, S. P., ... Pitman, R. K. (2011). Trauma reactivation under the influence of propranolol decreases posttraumatic stress symptoms and disorder: 3 open-label trials. *Journal of Clinical Psychopharmacology, 31*(4), 457-550. [ ]

Chambless, D. L., & Ollendick, T. H. (2001). Empirically supported psychological interventions: Controversies and evidence. *Annual Review of Psychology, 52,* 685-716. [ ]

Dudai, Y. (1996). Consolidation: Fragility on the road to the engram. *Neuron, 17(3),* 367-370. [ ]

Eichenbaum, H. (2002). *The cognitive neurosceince of memory.* New York: Oxford University Press. [ ]

Hermans, D., Craske, M. G., Mineka, S., & Lovibond, P. F. (2006). Extinction in human fear conditioning. *Biological Psychiatry,* 60(4), 361-368. [ ]

Hofmann, S. G., & Smits, J. A. (2008). Cognitive-behavioral therapy for adult anxiety disorders: A meta-analysis of randomized placebo-controlled trials. *Journal of Clinical Psychiatry,* 69(4), 621-632. [ ]

Hupbach, A., Gomez, R., Hardt, O., & Nadel, L. (2007). Reconsolidation of episodic memories: A subtle reminder triggers integration of new information. *Learning & Memory*, 14(1-2), 47-53. [ ]

Kandel, E. R. (2001). The molecular biology of memory storage: A dialogue between genes and synapses. *Science*, 294(5544), 1030-1038. [ ]

Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, severity and comorbidity of 12-month DSM-IV disorders in the National Co-morbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 62(6), 617-627. [ ]

Labrador, FJ, & Ballesteros, F. (2011). Effectiveness of treatments for social phobia in the applied field. *Psychothema*, 23(4), 560-565. [ ]

Labrador, FJ, Estupiñá, FJ, & García-Vera, MP (2010). Demand for psychological care in clinical practice: treatments and results. *Psychothema, 22* (3), 619-626. [ ]

LeDoux, J. E. (1999). *The emotional brain.* Barcelona: Planet. [ ]

Mineka, S., & Zinbarg, R. (2006). A contemporary learning theory perspective on the etiology of anxiety disorders. It's not what you thought it was. *American Psychologist, 61*(1), 10-26. [ ]

Misanin, J. R., Miller, R. R., & Lewis, D. J. (1968). Retrograde amnesia produced by electroconvulsive shock after reactivation of a consolidated memory trace. *Science, 160*(3827), 554-555. doi: 10.1126/science.160.3827.554 [ ]

Monfils, M. -H., Cowansage, K. K., Klann, E., & Le-Doux, J. E. (2009). Extinction-reconsolidation boundaries: Key to persistent attenuation of fear memories. *Science, 324*(5929), 951-955. [ ]

Nader, K., Schafe, G. E., & LeDoux, J. E. (2000a). The labile nature of consolidation theory. *Nature Reviews Neuroscience,* 1(3), 216-220. [ ]

Nader, K., Schafe, G. E., & LeDoux, J. E. (2000b). Fear memories require protein synthesis in the amygdala for reconsolidation after retrival. *Nature, 406*(6797), 722-726. [ ]

Roy-Byrne, P., Craske, M. G., Sullivan, G., Rose, R. D., Edlund, M. J., Lang, A. J., . Stein, M. B. (2010). Delivery of evidence-based treatment for multiple anxiety disorders in primary care: A randomized controlled trial. *JAMA. The Journal of the American Medical Association, 303*(19), 1921-1928. doi:10.1001/jama.2010.608 [ ]

Ruiz-Vargas, JM (2010). *Manual of memory psychology*. Madrid: Synthesis. [ ]

Schiller, D., Monfils, M. -H., Raio, C. M., Johnson, D. C., Ledoux, J. E., & Phelps, E. A. (2009). Preventing the return of fear in humans using reconsolidation update mechanisms. *Nature, 463*(7277), 49-53. [ ]

Sotres-Bayon, F., Cain, C. K., & LeDoux, J. E. (2006). Brain mechanisms of fear extinction: Historical perspectives on the contribution of prefrontal cortex. *Biological Psychiatry, 60*(4), 329-336. [ ]

Stewart, R. E., & Chambless, D. L. (2009). Cognitive-behavioral therapy for adult anxiety disorders in clinical practice: A meta-analysis of effectiveness studies. *Journal of Consulting and Clinical Psychology, 77*(4), 595-606. [ ]