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The lability of the acquired knowledge: Genesis and rebirth of the studies on the effect of reconsolidation[1]

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Abstract: A robust set of evidence demonstrates that, after reactivation, the memories incur a lability state, during which they are susceptible to manipulations that interfere in its content or on the probability of retrieval in the future. This effect, called "reconsolidation", is similar to the period of instability following the learning of new information, classically referred to as a "consolidation". Although the effect of reconsolidation is known for more than 40 years, the topic only received notoriety recently, and since then, an increasing number of scientific publications has elucidated some of the fundamental processes. However, once the theme has been little reported in the Brazilian literature, this article presents a critical review of the literature, which discuss the historical background of the reconsolidation concept, its methods of investigation, scope and prospects for research.

Keywords: reconsolidation, memory, cognition.

Introduction

The use of metaphors is abundant in cognitive psychology, and notable examples of use of these conceptual devices can be found in the science of human memory (Roediger, 1980). For example, the idea that memory is a "deposit" of information is one of the most recognizable descriptions between the cognitive sciences, and its beginnings can be traced back to the theory that proposes the existence of a double information storage system (Hebb, 1949): traces of short-term memory (short-term memory, MCP) are transformed into stable traces with prolonged duration (long-term memory, MLP).

The distinction between memory systems is due to the observation that experimental manipulations immediately performed after encoding information could interfere with the memory trace, whether it is modifying its contents, or by changing the probability of future retrieval. Once this initial lability period ends, the memory would definitely be stored in a long-term system. This description is used in the formalization of the consolidation, which, in its neurobiological version, describes a set of mechanisms responsible for the storage of memories, which occur both in the synaptic level and compared to different brain systems.

In the early 20th century, Müller and Pilzecker (1900) presented the first explanatory model on the observation that new memories could be selectively impaired, inspired by the observations of Ribot (1881) on selective short-term memory loss observed in amnesiacs. Müller and Pilzecker (1900) suggested that, in the "normal" functioning of the information storage system, immediately after the acquisition of new information, a phase of reactivations of the content learned would provide stability to the related memory. The eventual failure in carrying out this process (the example of amnesiacs) would necessarily lead to damages to the memory for the information recently learned, undermining the likelihood of future retrieval of its contents.

The classical studies of Müller and Pilzecker (1900) approached an effect currently known in the psychological literature as "retroactive interference". This phenomenon is related to the one-way interference of a material learned about another set of stimuli previously presented to participants. In addressing this theme, the authors used lists of syllables to demonstrate that retrieving information learned in a study phase could be undermined by certain experimental procedures, for example, the presentation of lists of additional syllables. From this, it was suggested that the "tendency to persevere" could serve to "consolidate" the information in the systems of representations of the participants.

Later, Hebb (1949) offered a physiological explanation for the description of Müller and Pilzecker (1900). The perseveration idea led Hebb to took the chance to enunciate a recurrent neural network activity that covers the new information was the factor that provided stability to the newly formed memory. This activity would also correspond to the system called as "short-term memory". In situations in which there is no interference in this neural activity, morphological changes in the synapses would become permanent connections between neurons activated in the recent learning, allowing to reactivate the same pattern in the future. This passage of information to a permanent state constituted the "long-term memory" on a dual model of Hebb.

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In the following decades, a broad set of evidences definitely established the assumption that memories are fragile and subject to change in the period immediately after the encoding. It was observed that this range of consolidation is critical to the consistency of memories, making them susceptible, for example, to electroconvulsive treatments (Duncan, 1949), to the administration of inhibitors of protein synthesis (Flexner, Flexner, & Stellar, 1965), or even to interference of related information (Gordon & Spear, 1973). However, any manipulations have an effect only if undertaken with sufficient temporal proximity to the presentation of the information. These observations, along with other empirical statements, constitute the hypothesis of synaptic consolidation (McGaugh, 1966), which constituted one of the most eloquent and widely accepted explanations for the formation of memories in the brain.

In view of this conceptual development, a perception on the memory as a system responsible for preserving the information from its initial acquisition, resulting in the popularization of the memory metaphor as a "deposit" of information. However, this metaphor carries a design of physical "stability", and although the empirical evidence suggest that the consolidation is the final process of formation of memories, in the 1970s a set of observations emerged, which came to challenge the hypothesis of synaptic consolidation in its assumption that the stabilization would be one-way, in which the memories carried over from an instability state to another stability state (but never the other way around).

Genesis of the studies on memory reconsolidation

The fundamental assumption related to the hypothesis of synaptic consolidation, i.e., the unidirectionality, had been undermined by research that showed that the consolidated memories could incur a state of fragility, in which they would be subject again to manipulations that would change the probability of future retrieval (e.g., Misanin, Miller, & Lewis, 1968; Robbins, & Meyer, 1970; Schneider & Sherman, 1968). Such studies have shown that the retrieval or the reactivation of a memory followed another period of stabilization, and this aspect is the first set of demonstrations of an effect that would be called "reconsolidation". This memory capacity to move from an inactive state to an active (and unstable) state has been regarded since then as one of the basic properties of memory.

Recently, the cognitive literature started to define this process as susceptibility of episodic memories to influences arising from the time the information is retrieved (Finn & Roediger, 2011; Finn, Roediger, & Rosenzweig, 2012; Lee, 2008, 2009; Nader, Schafe, & Le Doux, 2000; Sara, 2000). That is, the retrieval of episodic memories is not just a passive process of "reading" of the information previously stored. On the contrary, when an information is retrieved, to be available for the conscious memory, it incurs in a labile state, in which it is susceptible to modification or distortion (Finn & Roediger, 2011; Hardt, Einarsson, & Nader, 2010).

Interestingly, in the decades that followed the demonstration of the reconsolidation effect, and although the topic have demarcated its importance to the neurosciences, only a small number of researchers has developed a systematic program for the study (Hardt, Einarsson, & Nader, 2009; Sara, 2000). Recently, in a slashing example of Zeitgeist influence in the choice and the popularity of the objects of scientific study, the study publication of Nader, Schafe and LeDoux (2000) prompted the sudden revival of interest in the reconsolidation study, marking an inflection point on the quantity of research focused on the matter.

The "rebirth" of reconsolidation research

The publication of the article of Nader, Schafe and LeDoux (2000) served as a part on the recent interest of cognitive sciences on the "reconsolidation" topic. By studying the effects of reconsolidation in mice, the authors demonstrated that the memories of fear can be severely affected from the time they are retrieved. In the first step of the experiment (day 1), Nader and colleagues applied sets of pairs of tone-footshock in subjects of the sample, conditioning them to fear. Then (day 2, after 24h), an experimental group composed of half of the sample was reexposed only to tones, which prompted the sudden immobility behavior, indicating that the handling provided the retrieval of memory for events from the previous step (tone-footshock). All the rats, including half of the sample corresponding to the control group, whose memory for the shocks were not retrived, received a dose of an inhibitor of protein synthesis or its excipient. Finally (day 3), all the sample was tested for fear-related memories. The final results indicated that the sample whose memory was retrieved before injection of the inhibitory substance expressed less sudden immobility behavior than the rats whose retrieval followed the excipient administration and than individuals who were not subject to the retrieval of the memory for the tone-footshocks. The comparison with the latter group demonstrates that the retrieval of a memory is the essential aspect for the occurrence of the reconsolidation process.

The study of Nader, Schafe and LeDoux (2000) has shown that inhibiting substance of protein synthesis has blocked the reconsolidation process of retrieved memories and caused damages to the memory for fear – that is, the retrieval probability of memory in the future was decreased. It was possible to understand, from these results that the memory reactivation for fear provided the original memory return to a lability state similar to what is technically known as "consolidation", making the memory dependent on a new process of protein synthesis that returns the stability.

From the sudden profusion of neurobiological studies on reconsolidation occasioned by the publication of Nader, Schafe and LeDoux (2000), some research contemplated the study of this theme in the context of behavioral

approaches, until then an apparent disinterest in this object of study seemed to exist. The first investigation to experimentally demonstrate the reconsolidation effect on humans was performed by Walker, Brakefield, Hobson and Stickgold (2003), who studied the phenomenon in relation to procedural memory. Participants of the study of Walker and colleagues were initially trained in a procedural task of motor skills, which involved the typing of a simple numeric sequence (e.g., 5-6-8-7). After an interval of 24h, an experimental group was asked to test again the original numerical sequence before learning a new sequence (e.g., 2-4-3-7), while a control group learned only one new sequence, without recovering the original. Finally, after a new interval of 24h, a final test evaluated the performance of the participants to the original sequence of digits (5-6-8-7 in our example). Walker et al. (2003) showed that the performance was worst in the group that rehearsed the original sequence before learning the new one, in comparison with the group whose participants have not rehearsed the first sequence. This study showed that the reactivation of the memory for the original sequence prior to the new sequence (after 24h) made the memory susceptible to interference from a distinct motor pattern, it is possible to explain by the reconsolidation hypothesis.

After the demonstration of the reconsolidation effect on procedural memory by Walker et al. (2003), studies of Galluccio (2005) and Galluccio and Rovee-Collier (2005) extended the phenomenon study for the conditioning. The researchers trained babies to activate a mobile device from a movement with the leg (a kick). After an interval, the device was presented for a brief period during which was unlinked from the behavior (to kick), serving only as a clue for the reactivation of the original behavior. After this reactivation, a group of babies was trained to react similarly with other mobile device and a day after this procedure, this group has showed an alteration to the previously reactivated memory, since it no longer recognized the original mobile device, able to react only when presented in the second section of training.

Pioneering approaches in the field of experimental psychology by Walker et al. (2003), Galluccio (2005) and Galluccio and Rovee-Collier (2005) have in common the use of two forms of implicit memory, leaving open the study of the reconsolidation effect on explicit memories (i.e., semantic or episodic memories). Only two years later, the study of Hupbach, Gomez, Hardt and Nadel (2007) addressed the reconsolidation on explicit memory (in this case, episodic memories). Hupbach and colleagues presented a set of items (objects not related) in a first stage of the study (day 1). In a second phase (day 2), participants of the experimental group were asked to remind the event of the previous day (without requesting the recall of item to item); in the case of the control group, participants did not receive instruction to remind the previous step. Both groups were introduced to a new set of items. Finally (day 3), a free recall test investigated the performance of the subjects to for the set originally studied. Although the groups (experimental and control) do not present differences in performance in relation to the amount of items reminded on the test for the original list, Hupbach et al. (2007) have shown, from that procedure, that a significantly larger number of items belonging to the second set was incorrectly attributed to the original list (day 1), when participants were asked to briefly recall the event of the first day (the number of intrusions was greater for the experimental group). That is, the reactivation of the participants' memory for the original list (experimental group) promoted the memory return for the event to a lability state, which allowed the incorporation of new information.

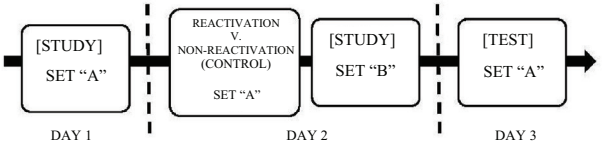

Figure 1. Basic scheme of a reconsolidation experiment with humans.
Typically, for the group which Set "A" is reactivated prior to the study with Set "B" (e.g. through a context tip), we observed a significantly larger number of intrusion of items belonging to Set "B" for the test with Set "A", when comparing with the group in which there is no reactivation.

Recently, Finn and Roediger (2011) investigated the reconsolidation effect in the interaction with the emotion (see also Finn, Roediger, & Rosenzweig, 2012). The authors investigated whether the benefits typically associated with the reconsolidation could be modulated by emotional events that occurred after the retrieval. In their study, the authors provide pairs of Swahili-English words for the study. Subsequently, the participants responded to a task of remembrance with clues, and each item correctly remembered was followed by a visual stimulus (photography), negative or neutral (or a blank canvas for the control condition). A final test of memory with clues evaluated the effects of stimuli provided after the retrieval step. The authors demonstrated that the memory is susceptible to interference even after the retrieval process. In addition, the emotional stimuli provided after memory retrieval improved the participants' performance, compared with neutral stimuli. That is, the emotionality of the post-retrieval events served as the performance modulator in a previous test, demonstrating that the reconsolidation mediated by emotional processing can increase the beneficial effects of episodic memory retrieval.

Theoretical aspects

In a review on the theme "reconsolidation", Nader and Einarsson (2010) showed three lines of evidence regarding the existence of a reestabilization period of memories after retrieval. First, it has been established that the subject's performance on memory tests can be impaired if anesthetics treatments are administered immediately

following the information reactivation (e.g., electrical stimulation, DeVietti, Conger, & Kirkpatrick, 1977; or pharmacological interventions, Blaiss & Janak, 2006). Secondly, the performance can be affected when new information interfere with sufficient temporal proximity, i.e. when they are provided after the retrieval of a memory, information that compete with the knowledge previously stored. Thirdly, the retention probability can be increased by means of some substances (e.g. strychnine). It is assumed that these manipulations are effective only when performed immediately after learning the new information, although recent evidence suggests that the declarative memory may be susceptible to interference in intervals of up to 48 hours (Chan & LaPaglia, 2013).

From these lines of evidence, two functions of adaptive nature have been suggested to explain the presence of the reconsolidation effect in humans. First, the reactivation of a memory allows the "update" of content related to it, to add new information or knowledge to the pre-existing memory (Lee, 2008; Nader & Einarsson, 2010; Sara, 2000).[2] Studies such as the Hupbach and colleagues (2007) have addressed and confirmed this functional aspect of the reconsolidation effect (see also: Hupbach, Gomez, & Nadel, 2009, 2011). Secondly, the retrieval of memories allows the modulation of memory trace force, increasing or decreasing the probability of subsequent retrieval. The studies of Finn and Roediger (2011) and Finn, Roediger and Rosenzweig (2012) fall in this perspective.

Assumptions about why a memory retrieval benefits the retention and increase the chances of a information to be properly retrieved, usually make reference to the retrieval process itself as being the main factor responsible for such benefits. However, there are disagreements about which mechanisms are involved in improving the retention. For example, McDaniel and Masson (1985) state that the information processing involved in the retrieval, whose character is elaborative, can by itself strengthen the memory trace. On the other hand, it is also possible that the number of routes used to recover a memory trace is increased as a memory is evoked (Bjork, 1975).

On the other hand, it is known that the lability and vulnerability arising from the reactivation of a memory depend on specific parameters (Lewis, 1979; Miller & Springer, 1973; Spear, 1973). In this sense, several approaches have investigated the boundaries within which the process of reconsolidation takes place. Several aspects seem to be involved in the event or in the effect of reconsolidation prevention, such as: the "age" of memory (Milekic & Alberini, 2002); the intensity of the training for specific information (Wang, Oliveira Alvares, & Nader, 2009); the consolidation of extinction (Eisenberg, Kobilo, Berman, & Dudai, 2003); the predictability of a stimulus reactivation (Lee, 2009); reactivation mode (direct or indirect; Debiec, Doyere, Nader, & LeDoux, 2006); among others. The investigation of such limits is directly related to the maturation of this research field, with a view to passage from the manipulation to the ability to forecast the effect occurrence, being this one of the precepts of any scientific approach.

Perspectives and final considerations

As Nader and Einarsson (2010) stated, a large limiter in modern theories related to reconsolidation is that these are mostly qualitative, once they are mainly investigating the relationship between consolidation and reconsolidation. In view of this, they are not able to do experimental predictions as to when and how a memory will incur or not in a process of reconsolidation (although exceptions can be found in studies such as Lee, 2009). It was observed very soon that not all the memories are susceptible to the effects related to the phenomenon under discussion, but the limits within which the effect occurs remain open, and that future research should explore this gap (Chan & LaPaglia, 2013; Lee, 2009).

Although the reconsolidation research have predominantly investigated basic aspects of the occurrence of the phenomenon, some approaches that focus on aspects targeted to applied research are notable. Some investigations illustrate the extent and possibilities for future research. For example, one of the areas in which the reconsolidation effect seems relevant is the treatment of Post Traumatic Stress Disorder (PTSD). One of the methods used is related to the administration of beta-adrenergic blockers, which are known to block the reconsolidation of fear conditioned in rats (Debiec & LeDoux, 2004), working directly in the amygdala. Pitman and Delahanty (2005) have suggested that the use of these agents can be effective in the treatment of acute trauma in humans. It is assumed that the Beta-Adrenergic receptors may act as amnesiacs during the reconsolidation process, and some promising data point to the need to invest in this approach (e.g., Miller, Altemus, Debiec, LeDoux & Phelps, 2004). Also, experimental approaches may be useful in the concept of new behavioral treatments for PTSD. Other clinical perspective related to the reconsolidation relates to the treatment of substance abuse. Lee, Di Ciano, Thomas and Everitt (2005) have shown that the interruption of the reconsolidation of memories related to substance abuse can interfere with the behavior of search for cocaine in rats, leading to similar studies in humans (pharmacological and behavioural).

However, the use of clinical approaches based on the reconsolidation effect is still dependent on a better theoretical understanding, especially due to the lack of clarity regarding the meaning of interrupting the reconsolidation process, both in cerebral level as behavioral level (Dudai, 2006). Other matters are related to these gaps in the area literature. For example, Dudai asks what is the scope of the reconsolidation effects in relation to the network of associations of the reactivated memory. Wouldn't be it plausible to conceive that all items associated with the retrieved

2 A divergent line research promotes the emphasis to the idea that the interferences from new information can represent a factor detrimental to the retrieved memory. From this concept, it is assumed that, at the time of retrieval, the memory is at the mercy of interference that decreases the likelihood that the original information was appropriately retrieved (Forcato, Rodríguez & Pedreira, 2007; Schiller et al., 2010).

memory will be affected by the administration of amnesiacs agents or similar behavioral approaches? You can use a similar questioning in relation to approaches that reinforce the memory trace (e.g., Finn & Roediger, 2011; Finn, Roediger, & Rosenzweig, 2012): would the entire network of associations be affected by the strengthening of reconsolidated memory?

The extension of the approaches of the reconsolidation effect can shed light to other phenomena traditional in the psychology literature. For example, it was suggested that the reconsolidation is behind the widely known suggestion effect of false information, widely studied from Loftus and Palmer (1974). This is a paradigm in which the false information is integrated into the memory of participants, which have great applicability, particularly, in Forensic Psychology and Testimony. This approach, as well as other experimental approaches, has as the key component the need of information retrieval, so that the relationship with the reconsolidation effect seems to be evident (Hardt et al., 2010).

Similarly, several effects that depend on the memory of information previously studied can be dependent on the reconsolidation effect (Hardt, Einarsson, & Nader, 2010). An example is the test effect (Roediger & Karpicke, 2006), widely known in the psychological and educational literature. This effect is related to the increased performance on memory tests as a result of the simple test of information previously studied (compared to the mere restudy of original information). Studies before the test effect (e.g., Bjork, 1975; McDaniel & Fisher, 1991; McDaniel & Masson, 1985; Tulving, 1967) stressed the importance of active recovery knowledge (as opposed to passive recovery, as occurs in restudy), although they differ in the explanation of the mechanisms by which the effect occurs. It is possible that the reactivation of the information, as well as its context, through testing, make them again labile and subject to effects typically attributed to the reconsolidation – among them, the improvement in retention.

There are no known surveys that investigate the reconsolidation in false memories, as the memories typically created from paradigms as DRM (Deese-Roediger-McDermott initials; Roediger & McDermott, 1995), in which associated word lists are presented to participants for study, eliciting, in a test phase, the false memory of words not studied, but associated with the original lists. Although it does not seem that it is likely that the reconsolidation effect is present in the genesis of false memories under the DRM paradigm (which, it is assumed, are due mainly to the effects of information encoding step; Roediger, Watson, McDermott, & Gallo, 2001), it is important to clarify if the false memories are also susceptible to the reconsolidation effect.

Finally, although the idea of constructive (and reconstructive) nature of the memory had been defined for more than 80 years (Bartlett, 1932), the revival of interest in the reconsolidation effect has been largely responsible for undermining the popular metaphor from the memory as a repository of information. According to Dudai (2009), although the memory is responsible for storing information about the past, its adaptive value allows the body to respond to future and past events. And it is exactly under this perspective of functionality and dynamism that it seems clear that there is a mechanism that allows for aggregate information to existing knowledge, or even allowing them to modify the relevance of the information stored.

A labilidade do conhecimento adquirido: gênese e renascimento dos estudos sobre o efeito de reconsolidação

Resumo: Um robusto conjunto de evidências demonstra que, após a reativação, as memórias incorrem em um estado de labilidade, durante o qual são suscetíveis a manipulações que interferem em seu conteúdo ou na probabilidade de recuperação no futuro. Esse efeito, denominado "reconsolidação", é similar ao período de instabilidade que se segue ao aprendizado de uma nova informação, classicamente referido como "consolidação". Embora o efeito de reconsolidação seja conhecido já há mais de 40 anos, apenas recentemente o tema recebeu notoriedade, e desde então um crescente número de publicações científicas tem elucidado alguns dos seus processos fundamentais. Porém, uma vez que o tema tem sido pouco divulgado na literatura nacional, este artigo apresenta uma revisão crítica de literatura, na qual se discutem os antecedentes históricos do conceito de reconsolidação, seus métodos de investigação, sua abrangência e as perspectivas de pesquisa.

Palavras-chave: reconsolidação, memória, cognição.

La labilité des connaissances acquises: études de la genèse et de la renaissance sur l'effet de la reconsolidation

Résumé: Un corps robuste de preuves démontre que, après la réactivation, les souvenirs encourent un état d'instabilité, au cours de laquelle ils sont sensibles aux manipulations qui interfèrent avec leur contenu ou de la probabilité de recouvrement. Cet effet, appelé "reconsolidation" est similaire au période d'instabilité que suit l'apprentissage d'une nouvelle information, classiquement appelé de "consolidation" . Bien que l'effet de la reconsolidation soit connu depuis plus de 40 ans, ce ne fut que récemment que la question reçue notoriété, et, depuis lors, un nombre croissant de publications scientifiques ont élucidé

certains de ses processus clés. Néanmoins. dés que le sujet a mérité peu d'attention dans la littérature nationale, ce document présente une revue critique de la littérature, où nous discutons l'histoire de la notion de reconsolidation, et des méthodes d'enquête, son champ d'application et perspectives de recherche.

Mots-clés: reconsolidation, mémoire, cognition.

La labilidad del conocimiento adquirido: La génesis y el renascimento de los estúdios sobre el efecto de reconsolidación

Resumen: Un cuerpo sólido de evidencias demuestra que después de la reactivación, las memorias incurren en un estado de labilidad, y durante este período son susceptibles a manipulaciones que interfieren en su contenido, o en la probabilidad de su futura recuperación. Este efecto, denominado "reconsolidación", es similar al período de inestabilidad que tiene lugar después del aprendizaje de una nueva información (lo que se denomina clasicamente "período de consolidación"). Aunque el efecto de reconsolidación se conoce desde hace más de 40 años, sólo recientemente este tema recibió notoriedad. A partir de entonces, un número creciente de publicaciones científicas ha lanzado luz sobre algunos de sus procesos fundamentales. Sin embargo, como el tema ha recibido poca atención en la literatura científica portuguesa, en este manuscrito presentamos una revisión critica de la literatura, y se discuten las raíces históricas del concepto de reconsolidación, los métodos de investigación, así como las direcciones futuras de la investigación sobre el tema.

Palabras clave: reconsolidación, memoria, cognición.

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