Behavioral Disruption of Memory Reconsolidation: From Bench to Bedside and Back Again

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During the postretrieval reconsolidation “window”, memories can be disrupted, strengthened, or updated using various pharmacological and behavioral manipulations. Behavioral manipulations are more ecologically valid, thus allowing better understanding of memory modification under natural conditions, but they can also be less potent compared to pharmacological interventions. In this review we present the current human and animal literature, aiming to understand the modulatory factors (i.e., task relevance, complexity, intensity) that promote reconsolidation disruption in purely behavioral means. The reviewed studies have suggested that both very simple tasks and more complex learning paradigms can be used to disrupt or update memory reconsolidation, even of stronger emotional memories. Stress exposure is a possible interference task, yet the conflicting results leave many open questions regarding its required timing and intensity. Going from bench to bedside and back again, we point to the need for more research in clinical populations to establish the therapeutic potential of reconsolidation-based treatments. Several findings from outside the laboratory offer promising leads for future research.

Keywords: anxiety, postretrieval extinction, PTSD, return of fear, stress

Newly formed memories are malleable and susceptible to interference until they stabilize in a process termed memory consolidation (Dudai, 2004). At the cellular level, the protein-synthesis-dependent process of consolidation is accomplished within the first minutes to hours after encoding (Kandel, 2001). However, even after this process is complete, memories are not set in stone. After retrieval, memories can become “reactivated”—return to a malleable state—until their restabilization (i.e., “reconsolidation”) is complete (Lewis, 1979; Misanin, Miller, & Lewis, 1968; see Figure 1 for illustration).

According to some assessments, the postretrieval reconsolidation “window” can last up to 6 hr (Schiller et al., 2010), during which memories can be disrupted (Nader, Schafe, & LeDoux, 2000), strengthened (Frenkel, Maldonado, & Delorenzi, 2005), or updated (Haubrich et al., 2015). The process of reconsolidation after retrieval is not identical to initial consolidation (Lee, Everitt, & Thomas, 2004; Taubenhof, Milekic, Monti, & Alberini, 2001). However, both processes share some underlying mechanisms (Alberini, 2005; Dudai, 2012), as demonstrated by their susceptibility to similar pharmacological interventions. For example, protein-synthesis inhibitors (e.g., anisomycin), which block protein synthesis at the synapse, prevent its required modification for consolidation and reconsolidation (Kandel, 2001; Nader et al., 2000). In addition, beta receptor antagonists (i.e., “beta blockers”), such as propranolol, which inhibit the amygdala-modulated noradrenergic activity (Roozendaal, Okuda, Van der Zee, & McGaugh, 2006), can prevent the consolidation or reconsolidation of new or retrieved emotional memories (Cahill, Prins, Weber, & McGaugh, 1994; Kindt, Soeter, & Vervliet, 2009). Apart from pharmacological interventions, both new and reactivated memories are susceptible to more naturalistic behavioral manipulations, for example, exposure to distractor stimuli or new information (Agren, 2014; Robertson, 2012).

Memory Reconsolidation: Relevance for Treatment

Memory reconsolidation is an update mechanism, allowing the animal to adapt to the changing environment (Alberini & LeDoux, 2013; Dudai, 2012). This constant modification of memories can explain why they may at times be unreliable (Loftus, 2003). In addition, this mechanism can offer potential noninvasive solutions for the treatment of several mental disorders, which are characterized by maladaptive memories. For instance, posttraumatic stress disorder (PTSD), which follows the occurrence of a highly aversive and traumatic event (Woud, Verwoerd, & Krans, 2017), is characterized by symptoms of reexposure, as well as avoidance and hyperarousal (American Psychiatric Association, 2013). Maladaptive memories are also seen in phobias, panic disorder, and obsessive–compulsive disorder, which all share a memory bias toward threat-related information (Coles & Heimberg, 2002). Distorted memory processes were also linked to addiction, which some authors have interpreted as a disruption in learning and memory of reward-related stimuli (Hyman, Malenka, & Nestler, 2006). In the laboratory, the classical conditioning paradigms of fear conditioning (LeDoux, 2000) and appetitive conditioning...
Behavioral Manipulation of Reconsolidation

The study of retroactive interference has been a long tradition in memory research, in particular for the consolidation of memory (Bäuml, 1996; Postman & Underwood, 1973; Robertson, 2012). It was suggested that memory interference is not a mere by-product of the competition between memories but an active process, independent from the processing of the individual memories. This process, mediated by areas in the frontal cortex (i.e., dorsolateral prefrontal cortex, primary motor area), allows memories, even of a different type (e.g., declarative and procedural memories), to interact and interfere with one another (Robertson, 2012). More recently, in the reconsolidation literature, various behavioral tasks have been used for the interference or update of emotional, declarative, and procedural memories after retrieval (Agren, 2014). We discuss the main findings in the next sections. Due to the relatively large number of studies (including both replication successes and failures), postretrieval extinction learning is discussed separately from other tasks as a particular case of postretrieval emotional memory interference—update. Then, in the last section, stress exposure is examined as a potential distractor—but also facilitator—of reactivated memories.

Interference and Update

In the late 1960s, the pioneering rodent study by Misanin et al. (1968) challenged the traditional view on memory, according to which memory consolidation is a one-time event (McGaugh, 1966). In their study, the group showed that a treatment of electroconvulsive shocks, administered after retrieval, leads to retrograde amnesia for already-consolidated fear memories. These findings suggested a more dynamic nature of memories than what was previously thought. As postulated later by Lewis (1979), a memory can become reactivated upon retrieval, that is, once again susceptible to interruption until its stabilization is completed and it becomes inactive. This intriguing idea had stayed out of the research mainstream for a long while and experienced a revival only after Nader et al. (2000) demonstrated retroactive protein-synthesis inhibitors treatment. In the last years, evidence has shown that reactivated memories can be affected not only by robust and invasive means, such as electroconvulsive shocks (Kroes et al., 2014; Misanin et al., 1968) or pharmacological treatments (Kindt et al., 2009; Nader et al., 2000) but also by behavioral tasks (Agren, 2014), both complex and simple.

New learning can be a robust postretrieval interference. Walker et al. (2003) demonstrated it in a neutral procedural task. On the first day, the participants were instructed to perform a sequential finger-tapping task (e.g., repeatedly tap the sequence 4–1–3–2–4 on a numeric keyboard). On the second day, the participants were tested on this sequence, showing the expected overnight (i.e., consolidation-based) improvement in accuracy and speed. Immediately after this recall test (i.e., reactivation), they learned a second sequence (e.g., the sequence 2–3–1–4–2). On the third day, the expected improvement in performance for the second sequence was evident, but the initial gains for the first, previously reactivated, sequence were lost. These findings showed that new learning can interfere with the reconsolidation of similar, earlier, memories that were returned in a labile state. The findings, however, raise two questions. First, is a similarity in content and complexity between the original (i.e., target) memory and the interfering task a crucial condition for interference? Second, are emotional memories likewise susceptible?
Simple Distractors and the Interference of Emotional Memories

In a study conducted by Schwabe and Wolf (2009), participants memorized a new story immediately after recalling neutral and emotional experiences from their recent past. Despite no apparent similarity between the memory and the interference task, the previously reactivated neutral memories were impaired. Emotional memories, however, were not affected. Emotionally arousing experiences are very well remembered compared to neutral events. This results from the interaction of glucocorticoids (GCs; mainly cortisol in humans, corticosterone in rodents) and noradrenaline in the basolateral amygdala, which in turn modulates the strength of memories in other brain areas (Roozendaal et al., 2006). In line with other works that showed interference effects only for neutral, and not emotional, material following behavioral treatment (Hupbach, Gomez, Hardt, & Nadel, 2007; Hupbach, Hardt, Gomez, & Nadel, 2008), Schwabe and Wolf (2009) thus suggested that mild behavioral manipulations might not be potent enough to disrupt emotional memories. In this case, more robust treatments may be needed. For instance, the beta blocker propranolol, which was able to impair the reconsolidation of strong fear memories in a subclinical population of spider-phobic individuals (Soeter & Kindt, 2015).

Nonetheless, James et al. (2015) demonstrated that even strong emotional memories can be affected by postretrieval behavioral interference. On the first day of this study, the participants watched a trauma film, a 12-min movie that consisted of 11 scenes capturing actual or threatened death or serious injury (e.g., a girl hit by a car, a man drowning in the sea). On the second day, the memory of the trauma film was reactivated by presenting the participants with a still picture from the film, taken moments before the aversive event. After a 10-min break, the participants engaged in a game of Tetris. The control groups were either given the memory reactivation task without the game, played the game with no prior reactivation, or were not exposed to any of the tasks. All participants then recorded intrusive memories for 7 days using a diary. A week later, intrusive memories were also recorded in the lab using a convergent measure (the intrusions-provocation task). In the reactivation-game group, the rate of intrusive memories was significantly lower compared to the case with the control groups. Consistent with the view of reconsolidation as an update mechanism (Alberini & LeDoux, 2013), both memory reactivation and playing Tetris were required to reduce the subsequent intrusions.

On a first glance, a game of Tetris seems to be very different from traumatic memories, thus suggesting that similarity in content or complexity between target and distractor are not crucial for interference. Nonetheless, both are similar in the demands they pose on cognitive processing, in particular on visual—spatial working memory. In detail, the memory of the trauma film consisted of mental images, such as visual scenes. The interference task, performed during the memory-reconsolidation window, was a visual—spatial task, and it thus competed with the trauma memory for working memory resources. The memory trace after disruption was, therefore, less vivid and intrusive. The findings of James et al. (2015) cannot, however, determine whether modality specificity is a necessary condition for emotional reconsolidation disruption.

In any case, it seems that a simple distractor could interfere with emotional memory reconsolidation, regardless of modality. For rats, a simple air puff might be sufficient. Crestani et al. (2015) trained rats in a contextual fear-conditioning task and 2 days later reexposed them to the training context (i.e., a reactivation session) in the presence or absence of a distractor stimulus. The distractor stimulus, an air puff from an empty bottle, was directed to the animal’s head and torso and was given every time the animal expressed the fear memory (i.e., freezing behavior). As a result, animals in the reactivation—air puff group showed a reduction in freezing behavior that lasted for up to 20 days. The long-lasting effect and the lack of spontaneous recovery suggested this was a reconsolidation-mediated effect. To test this directly, Crestani and colleagues prevented the reactivation—destabilization process, which is a necessary step triggering the reconsolidation process. Indeed, when the activation of selective L-type voltage-gated calcium channels or GluN2B-containing NMDA receptors in the hippocampus was prevented before retrieval, thus blocking memory destabilization (Ben Mamou, Gamache, & Nader, 2006; Suzuki, Mukawa, Tsukagoshi, Frankland, & Kida, 2008), the interfering air puff had no effect. It is unclear, however, which distractor tasks are simple yet robust enough to cause similar reconsolidation disruption in humans.

In sum, postretrieval learning, and even exposure to simple and seemingly unrelated tasks, were found to interfere with the reconsolidation of reactivated memories. Even though emotional memories are stronger than neutral memories, they might be susceptible to disruption using behavioral means as well. Future studies should investigate the role of working memory (e.g., the intensity of task and modality specificity) in postretrieval interference tasks, in particular for emotional memories.

Postretrieval Extinction

In standard extinction training, the individual learns that the previously acquired association is no longer valid (Rescorla, 1988). For instance, if a tone (conditioned stimulus [CS]) used to be paired with an electrical shock (unconditioned stimulus, or UCS), repeated exposures to the tone without the shock will gradually reduce the fear expectancy and response. The standard extinction learning creates a new inhibitory memory trace (CS—no UCS) that competes with the original fear memory trace (CS—UCS) but does not erase it (Bouton, 2004). Thus, if the fear memory regains dominance, relapse phenomena (generally termed return of fear) can be observed: spontaneous recovery after time elapse (Rescorla, 2004), renewal after context change (Bouton & King, 1983), or reinstatement after UCS exposure (Rescorla & Heth, 1975). Indeed, fear can return even after successful “exposure therapy,” an extinction-based treatment for anxiety and PTSD (Craske, 1999). The most intensely studied task for the interruption of emotional memory reconsolidation is the postretrieval extinction. Rather simple, this task involves performing the extinction training during the postretrieval reconsolidation window (Monfils, Cowansage, Klann, & LeDoux, 2009; Schiller et al., 2010). In contrast to standard extinction, this manipulation is suggested to lead to long-lasting, even permanent, effects (Björkstrand et al., 2015; Schiller, Kanen, LeDoux, Monfils, & Phelps, 2013).
10 min after reactivation) but not outside of it (6 hr after reactivation), no spontaneous recovery or reinstatement (Schiller et al., 2010) or renewal (Monfils et al., 2009) of fear are observed. Brain-imaging studies revealed the difference between postretrieval extinction and standard extinction. Unlike standard extinction, postretrieval extinction diminishes the involvement of the amygdala (Agren et al., 2012) and the prefrontal cortex (Schiller et al., 2013) in response to subsequent memory tests. In other words, following postretrieval extinction (and in contrast to standard extinction), the original fear memory is disrupted, perhaps even erased (Quirk et al., 2010). A follow-up study showed that this effect is long lasting in both the neural and behavioral levels (Björkstrand et al., 2015): The fear memory trace in the basolateral amygdala does not recover, and the fear response remains low, even 18 months posttreatment. Comparable results were found in animals, as postretrieval extinction was shown to reverse the fear-related synaptic strengthening in the amygdala (Clem & Huganir, 2010).

### Boundary Conditions and Limitations

The findings just described thus suggest postretrieval extinction as a safe and noninvasive therapeutic manipulation, ideal for the disruption of maladaptive emotional memories, both new and old (Steinfurth et al., 2014). However, several studies have reported replication failures in humans (Golkar, Bellander, Olsson, & Ohman, 2012; Kindt & Soeter, 2013; Meir Drexler et al., 2014) and rodents (Chan, Leung, Westbrook, & McNally, 2010; Goode, Holloway-Erickson, & Maren, 2017; Luyten & Beckers, 2017; Stafford, Maughan, Illoï, & Lattal, 2013). Indeed, some studies have found that postretrieval extinction leads to effects that are the opposite of those described by Monfils et al. (2009) and Schiller et al. (2010). For instance, Chan et al. (2010) demonstrated that a single reactivation trial before extinction augmented the retrieval and reinstatement of the extinguished response. This enhancement of fear relapse was not observed if the reactivation and extinction took place in two different contexts. Similarly, Stafford et al. (2013) found that extinction learning during the fragile postretrieval period leads to an impaired extinction.

Memory reactivation (and the subsequent reconsolidation process) does not occur each and every time a memory trace is retrieved (Judge & Quartermain, 1982; Sevenster, Beckers, & Kindt, 2013). It requires a “prediction error” between what was expected and what actually happened (Fernández, Boccia, & Pedreira, 2016; Sevenster, Beckers, & Kindt, 2012; Sevenster et al., 2013). Triggering this update mechanism is assumed to depend on specific parameters, generally called “boundary conditions.” Among them are memory-related factors (e.g., type, age, and strength of the memory) and reactivation-related factors (i.e., different conditions that affect the degree of memory destabilization: Auber, Tedesco, Jones, Monfils, & Chiamulera, 2013; Wichert, 2012). The replication failures in achieving an effect using the postretrieval extinction paradigm suggest that this manipulation might be particularly sensitive to potential boundary conditions, such as the initial strength and type of the memory (Kredlow et al., 2016; Soeter & Kindt, 2011; Suzuki et al., 2004) and contextual factors (Chan et al., 2010; Kredlow et al., 2016; Stafford et al., 2013). Moreover, it has been suggested that some forms of relapse (e.g., reinstatement, spontaneous recovery) or fear responses (e.g., startle response) might be more amenable than are others (Goode et al., 2017; Kindt et al., 2009; Kredlow et al., 2016).

Gershman, Monfils, Norman, and Niv (2017a, 2017b) proposed that two mechanisms interact to produce reconsolidation: an associative learning mechanism and a structure-learning mechanism that segments the stream of experience into statistically distinct clusters (i.e., “latent causes”). Memory modification is possible only when the latent cause of the original memory (“acquisition”) is active (as presumably occurs in successful reconsolidation interventions); otherwise, a new latent cause (e.g., “extinction”) is created (as occurs in standard extinction). This model, they suggested, can explain the nature of the reconsolidation process and its boundary conditions (such as memory age) and account for some of the replication failures in the postretrieval extinction paradigm.

Replication failures may also result from lack of standardization in methodological choices across different research groups. This issue was thoroughly discussed in a recent review on fear conditioning and extinction (Lonsdorf et al., 2017). For instance, Schiller et al. (2013), who found a beneficial effect of postretrieval extinction, excluded participants who showed an initial extinction deficit. This not only limits the ecological validity of the findings (extinction deficit is seen in anxiety and PTSD patients; Maren & Holmes, 2016) but also can explain failures to replicate these findings in studies that did not use this exclusion criterion.

### Stressor: Distractor or Facilitator?

A stressor is a physical or psychological challenge that exceeds the natural regulatory capacity of the animal. The resulting “stress response,” mediated by monoamines (e.g., noradrenaline) and GCs, promotes the animal’s adaptive physiological and behavioral response (Joëls & Baram, 2009). Like newly acquired memories (Roozendaal, 2000), reactivated memories appear to be sensitive to stress manipulations as well (Akirav & Maroun, 2013), yet the direction of the effect is still debated (Shields, Sazma, McCullough, & Yonelinas, 2017). For instance, whereas several studies demonstrated memory impairment following postretrieval stress treatment (Dongaonkar, Hupbach, Gomez, & Nadel, 2013; Schwabe & Wolf, 2010; Wang, Zhao, Ghitza, Li, & Lu, 2008; Zhao, Zhang, Shi, Epstein, & Lu, 2009), others showed facilitative effects (Bos, Schuijer, Lodestijn, Beckers, & Kindt, 2014; Cheung, Garber, & Bryant, 2015; Coccoz, Maldonado, & Delorenzi, 2011). Even within the group of studies that found disruptive effects of stress on memory reconsolidation, emotional memories differed in their relative sensitivity to the manipulation: either more sensitive than neutral memories (Zhao et al., 2009) or not sensitive at all (Schwabe & Wolf, 2010).

### Modulating Factors of the Effects of Stress

In the general reconsolidation literature, several factors have been suggested to influence the direction and strength of reconsolidation effects: memory-related factors (e.g., memory age, type, and strength), manipulation-related factors (i.e., the reactivation and treatment methods), and individual differences (e.g., sex, trait anxiety; for a review, see Meir Drexler & Wolf, 2017a). The limited number of studies on reconsolidation—stress and their conflicting findings leave many open questions (Shields et al., 2017) that should be targeted in future research. Three such questions are mentioned next.
1. Does the modulatory effect of stress on memory reconsolidation depend on exact timing? Larrosa et al. (2017) suggested that the long-term improving effects of stress on memory reconsolidation occur if the autonomic response takes place shortly after the initiation of the reconsolidation process. That is, memory improvement is expected in the case of postretrieval stress (Cocuzzo et al., 2011). In contrast, when memory reactivation takes place 20–30 min after stress, the autonomic response is no longer present (Joëls & Baram, 2009), and the isolated cortisol effects could account for the long-term impairing effects on memory reconsolidation. That is, memory impairment is expected in the case of preretrieval stress (Larrosa et al., 2017; Meir Drexler & Wolf, 2017b).

2. Does the modulatory effect of stress depend on intensity levels? Dodd and Lukowiak (2015) trained snails in an operant conditioning paradigm of aerial respiratory behavior. When this operant memory was reactivated and followed by multiple stressors (both handling and crowding), the snails’ performance was impaired, presumably due to reconsolidation disruption. In contrast, the postretrieval presentation of either of the stressors alone did not affect memory reconsolidation. The results suggest that a certain level of stress intensity is needed to affect reconsolidation. This account might explain why some stressors have not been effective in modifying reconsolidation in some studies (Shields et al., 2017). However, the predictive value of this account, in particular for human studies (i.e., what is the “right” amount of stress?), has to be further investigated.

3. Can stress be implemented in future therapeutic reconsolidation-based interventions? Stress timing in relation to retrieval can be easily modified in treatment, but if intense stress is required for it to create a significant interruption to the reactivated memory (Dodd & Lukowiak, 2015), it is not ideal for therapy. However, even mild stressors can be successfully used for the disruption of emotional memory reconsolidation (Zhao et al., 2009) in humans.

We have recently found that exposure to a mild stressor (the socially evaluated cold-pressor test, or SECPPT) 30 min before reactivation disrupts the reconsolidation of fear memories in healthy men (Meir Drexler & Wolf, 2017b). This disruptive effect was contrary to the enhancing effect of cortisol administration found earlier using the same design (Meir Drexler, Merz, Hamacher-Dang, Tegenthoff, & Wolf, 2015). Indeed, the two manipulations differed in the resulting cortisol levels (very high following hydrocortisone intake, moderate following stress exposure) and noradrenergic involvement (present following stress exposure, absent following pill intake). However, viewing the stress exposure as a new learning episode might provide a more convincing explanation for this discrepancy. The stressor presents a more complex, possibly emotional, learning experience compared with the benign experience of pill intake. Like other emotional experiences, stressful events are better remembered compared with neutral events (Roozendaal, 2000). The emotional event could thus lead to interference (Cadle & Zoladz, 2015), thereby disrupting the reconsolidation of the reactivated memory. Strange, Kros, Fan, and Dolan (2010) found similar results using a simple postretrieval emotional stimulus. In this study, participants reactivated the memory of previously learned nouns and then were presented with pictures of faces, either fearful or neutral. The memory for reactivated nouns, which were followed by a fearful (but not neutral) face, was impaired at a later test. This effect was even stronger when the nouns themselves were of an emotional valance. These findings thus suggest that even a mild stress or an emotional stimulus might be potent enough to disrupt emotional memory reconsolidation.

Conclusion

The studies reviewed so far demonstrate that it is possible to update or disrupt neutral or emotional memories using purely behavioral means: simple distractors, more complex learning tasks (including extinction learning), and stress exposure (for a summary, see Table 1). Can these promising findings be used in therapy? In the next section, we go from bench to bedside (and vice versa) to investigate the clinical potential of reconsolidation-based behavioral manipulations.

Clinical Implications of Reconsolidation-Based Behavioral Manipulations

From Bench to Bedside

The reactivation-dependent lability of the memory trace was suggested to serve as an adaptive updating mechanism, allowing the modulation of memories after retrieval (Alberini, 2011; Alberini & LeDoux, 2013). This postretrieval mechanism can explain why some memories become distorted over time (Edelson, Sharot, Dolan, & Dudai, 2011; Loftus, 2003). A better understanding of the dynamic process of memory reconsolidation may also have therapeutic implications, contributing to the treatment of several psychiatric disorders, such as PTSD, phobias, and addictions. Because reconsolidation manipulations are thought to affect the original memory itself (Agren, 2014; Schiller et al., 2013), they have great potential in preventing relapse.

An ideal reconsolidation-based intervention has to be potent enough, but not aversive, and lead to long-lasting effects. Among purely behavioral manipulations, postretrieval extinction (Monfils et al., 2009; Schiller et al., 2010), mild forms of stress (Meir Drexler & Wolf, 2017b), and the use of distracting stimuli (James et al., 2015) can be potential nonaversive candidates. However, like the vast majority of reconsolidation studies, these studies were conducted on animals or healthy human participants and not clinical populations. Moreover, even though some authors suggested that reconsolidation deficits might be less persistent or effective compared to consolidation deficits (Judge & Quertermun, 1982; Parsons & Davis, 2011; Stafford & Lattal, 2009), the long-term (i.e., months, years) effects of these interventions are rarely investigated (for exceptions, see Björkstrand et al., 2015; Schiller et al., 2010). Nonetheless, several studies showed that reconsolidation-based behavioral or pharmacological treatments could indeed affect maladaptive memories in some target populations. For instance, Soeter and Kindt (2015) showed fear memory disruption in...
subclinical spider-phobic individuals following propranolol treatment, and Zhao et al. (2009) demonstrated memory impairment in drug-related words following reactivation and stress treatment in abstinent heroin addicts. Nevertheless, more evidence is needed, in particular in the case of PTSD. Current findings have suggested that it is more difficult to target and disrupt the complex memory traces in PTSD (compared to the relatively simple memory trace in phobias) using reconsolidation-based interventions (Surís, North, Adinoff, Powell, & Greene, 2010; Wood et al., 2015). Therefore, the effects are short term at best (Surís et al., 2010).

If one steps out of the laboratory, however, one might encounter some evidence of the possible utilization of reconsolidation in psychotherapeutic work (Bolitho, 2017; Ecker, 2015; Ecker, Titic, Hulley, & Neimeyer, 2012; Shapiro, 2002).

From Bedside to Bench

The reconsolidation process may be the underlying mechanism in some commonly used practices, either intentionally (Ecker et al., 2012) or unintentionally (Shapiro, 2002; see Table 2). Ecker et al. (2012) integrated the reconsolidation paradigm into a framework of coherence therapy, thereby developing the memory reconsolidation therapy. Here, after the identification of distressing events, emotions, and beliefs (i.e., the target memories) and the exploration of contrary experiences (i.e., the new material), a memory reconsolidation process is triggered. Following the reactivation of memory (i.e., retrieval session), the therapist encourages the client to acknowledge the mismatch. Indeed, prediction error is critical for memory reactivation following retrieval (Fernández, Pedreira, & Boccia, 2017; Sevenster et al., 2013). As a result of this intervention, the negative patterns of thinking—feeling—behaving are reduced.

Other practices might be, unintentionally, based on memory reconsolidation as well. Eye movement desensitization and reprocessing (EMDR) is a psychotherapy approach in which the patient focuses on traumatic memories while simultaneously making lateral eye movements (Shapiro, 2002). EMDR is used for reducing anxiety, depression, and dissociative symptoms, and according to some reports, it is as effective as prolonged exposure therapy (Rothbaum, Astin, & Marsteller, 2005). The reported success but poor theoretical rationale has made this treatment the focus of

### Table 1

**Behavioral Manipulation of Reconsolidation in the Lab**

<table>
<thead>
<tr>
<th>Postretrieval manipulation</th>
<th>Effect on the reactivated memory</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>New, unrelated story</td>
<td>Memory of neutral (but not emotional) autobiographical events was impaired.</td>
<td>Schwabe and Wolf (2009)</td>
</tr>
<tr>
<td>Neutral or fearful faces</td>
<td>Memory of previously learned nouns (in particular, emotional ones) was impaired when the distractor was emotional (but not neutral).</td>
<td>Strange et al. (2010)</td>
</tr>
<tr>
<td>Computer game</td>
<td>Rate of intrusive memories from a trauma film was decreased.</td>
<td>James et al. (2015)</td>
</tr>
<tr>
<td>Postretrieval extinction</td>
<td>Long-term reduction in fear behavior, original fear memory was disrupted at the neural level. However, several studies showed no effect.</td>
<td>Agren et al. (2012); Schiller et al. (2013, 2010); Golkar et al. (2012); Kindt and Soeter (2013); Meir Drexler et al. (2014)</td>
</tr>
<tr>
<td>Stress induction</td>
<td>Memory impairment but conflicting results regarding the effect on emotional memories. Stress intensity and timing (i.e. pre-retrieval) might also play a role. However, several studies showed memory enhancement.</td>
<td>Schwabe and Wolf (2010); Zhao et al. (2009); Dodd and Lukowiak (2015); Larrosa et al. (2017); Meir Drexler and Wolf (2017b); Bos et al. (2014); Coccoz et al. (2011)</td>
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### Table 2

**Evidence for the Utilization of Reconsolidation Processes in Psychotherapeutic Work**

<table>
<thead>
<tr>
<th>Practice</th>
<th>Suggested effect on maladaptive memories</th>
<th>References</th>
</tr>
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<tbody>
<tr>
<td>Memory reconsolidation therapy</td>
<td>After the identification of emotions and beliefs and distressing events (i.e., the target memories) and contrary experiences (i.e., the update material), a memory reconsolidation process is triggered (i.e., a reactivation session). The therapist encourages the client to acknowledge the mismatch. As a result, the negative patterns of thinking—feeling—behaving are reduced.</td>
<td>Ecker et al. (2012)</td>
</tr>
<tr>
<td>Eye movement desensitization and reprocessing</td>
<td>This practice involves the retrieval of traumatic memories and the use of distractors (lateral eye movements). It is suggested that the taxing eye movements impair the reconsolidation of the reactivated memories. Used for reducing anxiety, depression, and dissociative symptoms.</td>
<td>Shapiro (2002); Shapiro and Maxfield (2002)</td>
</tr>
<tr>
<td>Restorative justice practices</td>
<td>An exposure to the perpetrator (in a safe and mediated space) might trigger the reactivation of the traumatic event. Then, the mismatch between expectation and reality allows for the update of memory, leading to a long-lasting reduction in negative emotions relating to the event.</td>
<td>Bolitho (2017)</td>
</tr>
</tbody>
</table>
extensive debate and criticism. EMDR involves memory retrieval and the use of distractors, and so reconsolidation disruption was suggested as a possible underlying mechanism (Shapiro, 2002; Shapiro & Maxfield, 2002). According to this account, the reactivated trauma memories become susceptible after retrieval, and their reconsolidation is disrupted by the taxing eye movement, making the reconsolidated memories less vivid and desensitized. This account is in line with the previously reported findings on the effects of distractors on reactivated memories in healthy participants (James et al., 2015) and animals (Crestani et al., 2015). Additional studies have suggested that the more difficult the working memory task, the larger the disruptive effects (e.g., Littel, Remijn, Tinga, Engelhard, & van den Hout, 2017a, 2017b). It is interesting that, in addition to memory-reconsolidation therapy and EMDR, reconsolidation mechanism was also suggested to account for some of the beneficial emotional impacts of restorative justice practices (Bolitho, 2017). In this victim-oriented practice, exposure to the perpetrator (in a safe and mediated space) might trigger the reactivation of the traumatic event. Then, the mismatch between expectation and reality allows for the update of memory, leading to a long-lasting reduction in negative emotions relating to the event (Bolitho, 2017). Future studies are needed to directly test the reconsolidation account for these cases using the required control groups.

Concluding Remarks

In conclusion, significant evidence has supported the susceptibility of reactivated memories to purely behavioral manipulations following retrieval. Indeed, either very simple working memory tasks or more complex learning paradigms can be used to disrupt or update memory reconsolidation. Even though emotional memories are stronger than neutral memories, and thus theoretically less susceptible to disruption, some behavioral manipulations are robust enough to impair them as well. Nonetheless, a better understanding of the underlying mechanisms as well as the additional factors that influence the direction—strength of reconsolidation manipulations is needed, in particular in the case of stress. Most important, more studies in clinical populations are needed to investigate the therapeutic potential of reconsolidation-based behavioral manipulations. Several findings from outside the laboratory provide some promising leads for future research.

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