Archival Report

Biological Psychiatry

An Abrupt Transformation of Phobic Behavior After a Post-Retrieval Amnesic Agent

Marieke Soeter and Merel Kindt

ABSTRACT

BACKGROUND: Although disrupting the process of memory reconsolidation has a great potential for clinical practice, the fear-amnesic effects are typically demonstrated through Pavlovian conditioning. Given that older and stronger memories are generally more resistant to change, we tested whether disrupting reconsolidation would also diminish fear in individuals who had developed a persistent spider fear outside the laboratory.

METHODS: Spider-fearful participants received a single dose of 40 mg of the noradrenergic β-blocker propranolol ($n = 15$), double-blind and placebo-controlled ($n = 15$), after a short 2-min exposure to a tarantula. To test whether memory reactivation was necessary to observe a fear-reducing effect, one additional group of spider-fearful participants ($n = 15$) received a single dose of 40 mg propranolol without memory reactivation.

RESULTS: Disrupting reconsolidation of fear memory transformed avoidance behavior into approach behavior in a virtual binary fashion—an effect that persisted at least 1 year after treatment. Interestingly the β-adrenergic drug did initially not affect the self-declared fear of spiders but instead these reports followed the instant behavioral transformation several months later.

CONCLUSIONS: Our findings are in sharp contrast with the currently pharmacological and cognitive behavioral treatments for anxiety and related disorders. The β-adrenergic blocker was only effective when the drug was administered upon memory reactivation, and a modification in cognitive representations was not necessary to observe a change in fear behavior. A new wave of treatments that pharmacologically target the synaptic plasticity underlying learning and memory seems to be within reach.

Keywords: Anxiety disorders, Fear memory, Propranolol, Reconsolidation, Spider phobia, Treatment

http://dx.doi.org/10.1016/j.biopsych.2015.04.006

Fear memories are no longer considered as indelible entities. During past years, it was rediscovered that retrieval of a consolidated fear memory may instigate a protein synthesis–dependent restabilization process called reconsolidation (1). Pharmacological disruption of this process enables the modification of a previously acquired fear memory. In the laboratory, specific fear memories can be established through Pavlovian fear conditioning, which involves the repeated pairing of an initially neutral cue (e.g., a tone or picture; conditioned stimulus, CS) with an inherently noxious stimulus (e.g., an electric stimulus; unconditioned stimulus, US). As a result, an associative memory trace is being formed and the later presentation of the CS will retrieve the US representation, thereby eliciting a conditioned fear response. An important asset of the fear-conditioning paradigm is that it is well-suited to investigate the neurobiological mechanisms underlying associative fear learning and memory across species (e.g., crabs, rats, and humans). Fear conditioning is also an excellent translational model to develop, and advance treatment given that anxiety disorders are by definition irrational (2) and refer to learned fears as opposed to innate fears. Although associative fear memory lies at the core of fear and anxiety disorders (3), it bears mentioning that anxiety disorders do not necessarily result from direct conditioning experiences such as traumatic events. Fear memory may also result from indirect or vicarious fear learning experiences (4). However, irrespective of the learning history, people with anxiety disorders act as if the feared stimulus (e.g., heart palpitations) predicts the later occurrence of a negative outcome (e.g., panic attack or heart failure). Insofar as associative fear memory is regarded as the core of anxiety disorders (5), it not only entails predictive learning in which the originally neutral or ambiguous stimulus (CS) becomes a valid predictor for a negative experience (US) but also that this feared stimulus is endowed with a negative valence through its association with the negative consequence (US) (6,7).

Insights on disrupting reconsolidation of fear memories may point to an efficient strategy for the treatment of anxiety disorders and posttraumatic stress disorder (8). By now, the fear-erasing effect has been replicated in a variety of species and paradigms (9). A series of human fear-conditioning studies showed that disrupting reconsolidation by the noradrenergic β-blocker propranolol HCl neutralized the fear memory (10–13) while leaving the expectancy learning unaffected. Propranolol HCl passes the blood-brain barrier and is supposed to block the β-adrenergic receptors in the amygdala, thereby interfering with the PKA-CREB pathway involved in the neuroplasticity of memory (14,15). However, experimental models of human fear conditioning are an oversimplification of the emotional memory characteristic for pathological fear and its related

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 ISSN: 0006-3223

disorders (5,16–18). It may therefore be questioned whether the current procedure of disrupting memory reconsolidation can be effectively applied to people with fear and anxiety disorders (2). First, the fear-erasing effects in humans have most convincingly been demonstrated for relative young (1 day old) and weak fear memories, because human fear conditioning involves only a mild noxious experience. From the animal literature, it is known that the activation of the reconsolidation process appears to be dependent on both the age and strength of memories, in which older and stronger memories become increasingly resistant to disruption (19). On the other hand, preliminary evidence in patients with posttraumatic stress disorder revealed a reduction in trauma-relevant physiological responding after a β-adrenergic interference with reconsolidation (8), but this effect could not be replicated (20). A second potential boundary condition relates to the fact that fear memories in people with anxiety disorders are generally broader and less well-defined than the simple fear association between a specific stimulus (e.g., picture) and a single aversive event (e.g., electric stimulus) installed by a Pavlovian fear-conditioning procedure. In previous fear-conditioning studies, we demonstrated that the fear-reducing effect was not restricted to the reactivated stimulus but also generalized to other stimuli from the same semantic category, not previously associated with the originally conditioned stimulus (11,12). However, strengthening fear memory by either variation in training intensity (21) or pharmacologically induced CREB phosphorylation (12,22,23) triggers a broader fear generalization. Therefore, it remains unclear whether older, stronger, and broader fear memories acquired outside the laboratory are also sensitive to a memory reconsolidation intervention. Another challenge for clinical applications is that the anticipated threat event does not necessarily involve a circumscribed threat event such as in a Pavlovian fear-conditioning procedure. In many cases, people tend to fear objects and situations that they have never really experienced (4). Although we have shown that disrupting reconsolidation also erased fear for a noxious event (i.e., electrical stimulus) that was anticipated but never actually experienced (24), the anticipated catastrophe in people with anxiety disorders does not necessarily refer to external events but may also refer to aversive feelings such as the fear of losing control (25,26).

In sum, a key question is whether targeting fear memory by amnesic agents will be of value for clinical practice. For addressing this question, we tested whether disrupting reconsolidation by a noradrenergic β-blocker also diminishes fear responding in individuals who have spider phobia. In fear-conditioning studies, it was demonstrated that reconsolidation occurs when a retrieval session involves an event that 1) generates an expectation of threat (27) and 2) initiates new learning—meaning that the magnitude of the outcome or the outcome itself is not being fully predicted (i.e., a prediction error) (13,28). However, a retrieval session that engages "too much" learning might not trigger destabilization of an original fear memory but forms a boundary condition even before fear extinction can be observed (29,30). Bearing these points in mind the spider-fearful participants were very briefly exposed to a tarantula while they were in the supposition that they had to touch the spider, but, in reality, this never happened, to prevent possible extinction learning. After the participants were exposed to the tarantula for only 2 minutes, the therapist closed the terrarium. We assumed that this short exposure session would trigger destabilization of the associative fear memory (i.e., spider ≥ aversive consequence) and prevent the risk of inducing fear extinction (29,30). After this brief exposure, the participants received (double-blind and placebo-controlled) a single oral dose of 40 mg of propranolol HCl, a β-adrenergic receptor antagonist known to disrupt memory reconsolidation (10–13). For discarding any nonspecific dampening effects of propranolol HCl on the degree of spider fear, the drug was administered (single-blind) to a third group of spider-fearful participants without the memory reactivation (MR) session. For assessing the degree of spider fear, we used self-report assessments as well as two behavioral approach tasks. The experimental design is shown in Figure 1.

METHODS AND MATERIALS

Participants

A total of 45 healthy individuals,[1] 41 women scoring >17 on the Spider Phobia Questionnaire (31) and ranging in age from 18–32 years (mean ± SD age, 21.6 ± 3.2 years), were referred for the study. Participants were randomly assigned to either the propranolol HCl (n = 15, 13 women) or the pill placebo group (n = 15, 14 women). An additional propranolol no-reactivation group was also included (n = 15, 14 women) for discarding any nonspecific dampening effects of the propranolol drug (Table S1 and Supplement).

Assessments

Questionnaires. For obtaining an assessment of the self-reported spider fear, the Spider Phobia Questionnaire was administered, consisting of 31 items to be rated true or false (31). Participants rated on 0- to 8-point scales the credibility of the standard behavioral therapy for spider phobia (i.e., exposure) as well as the experimental treatment with propranolol.

Behavioral Tests. Behavioral approach tests (i.e., BATs) were used to assess the degree of fear while being exposed to a spider as well as overt approach behavior toward spiders. See the Supplement for details on the phobic stimuli.

Pre- and Posttreatment Assessments with Baby Tarantula (t0, t3, t4, t5). A baby tarantula was placed in a closed jar on a table in the far end of a 3.5 × 5-m room. Participants were instructed to enter the room and to accomplish each step of the standardized baby-tarantula BAT within 3 minutes, but they were free to stop the test at any point (Table 1). Behavioral approach ratings ranged from 0 to 8, corresponding to the last accomplished step. Participants were further required to rate their level of fear or anxiety by using 0- to 100-point scales (32) at each completed step: 0 = no fear,

[1]A sample size of 15 participants per group was considered to be adequate based on a power analysis of our previous fear conditioning studies (10–13).

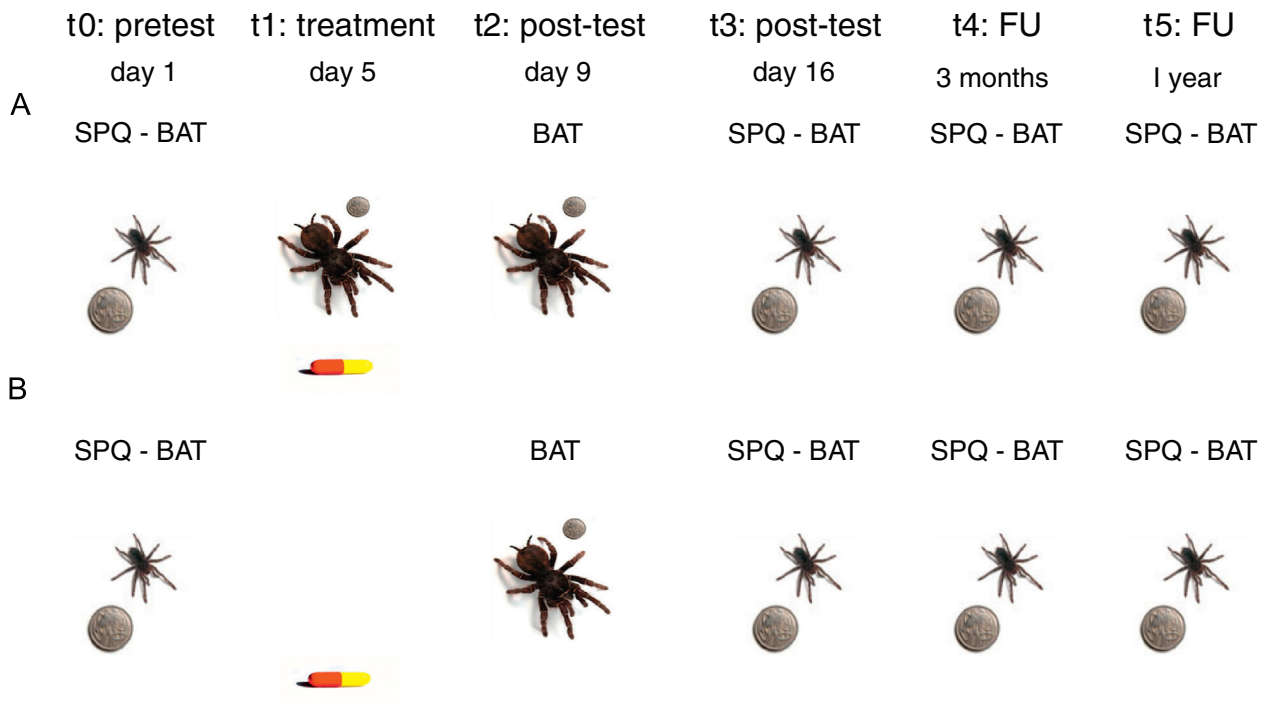

Figure 1. Schematic representation of the experimental design for **(A)** the MR_propranolol and MR_placebo group and **(B)** the propranolol group. BAT, behavioral approach task; FU, follow-up; MR, memory reactivation; SPQ, Spider Phobia Questionnaire.

25 = mild fear, 50 = moderate fear, 75 = severe fear, and 100 = very severe fear.

Posttreatment Assessment With Tarantula (t2). Participants stood in front of an open-caged tarantula at a distance of approximately 60 cm and were asked to approach and attempt to touch the spider with their bare fingertips. Approach behavior was defined as the nearest proximity toward the tarantula: 0 = staying at a distance of 60 cm from the tarantula, 1 = standing at a distance of 30 cm from the spider, 2 = standing at the front of the container at 0 cm, 3 = touching the container, 4 = dangling a hand inside the container, and 5 = touching the tarantula (33). At the point of nearest proximity, the participants were asked to rate their level of fear by using the 0- to 100-point scales.

Table 1. Steps of the Standardized Baby-Tarantula BAT

Step	Instructions BAT
1	Sit in front of a spider that is in a closed jar at a distance of 20 cm.
2	Hold the palm of your hand on either side of the closed jar for at least 10 seconds.
3	Open the jar with the spider.
4	Pick up the open jar with the spider for at least 10 seconds.
5	Direct the spider's movement in the jar with a pencil for at least 10 seconds.
6	Put the spider in a tummy-tub.
7	Follow the spider with a bare finger as it crawls around the tummy tub for at least 10 seconds.
8	Let the spider walk on your bare hands.

BAT, behavorial approach task.

Procedure

Researchers. One undergraduate research assistant (WC) accomplished all pretreatment tests. Another research assistant (NS) performed all posttreatment tests. Under the supervision of MS (i.e., first author), both research assistants received extensive training with the protocol and practiced on a number of participants before running experimental participants. MS carried out all treatments under the supervision of MK (i.e., corresponding author) (clinical registration No. 39051566025). All the researchers were blind to the conditions.

Pretreatment Assessments and BAT With Baby Tarantula (t0). Participants read an information sheet describing the treatment study (see Supplement for a detailed description). Once a participant was medically cleared, the Spider Phobia Questionnaire (31) as well as the State-Trait Anxiety Inventory (34), the Anxiety Sensitivity Index (35), the Beck Depression Inventory (36), and the treatment credibility ratings were administered. Subsequently, the participants were instructed regarding the baby-tarantula BAT, and the test was performed. Participants who were able to touch the baby tarantula during this initial BAT were excluded from further testing.

Assessments and Treatment (t1). Blood pressures as well as salivary samples were collected. Furthermore, the specific phobia section of the Structured Clinical Interview for DSM-IV (37) was administered, which allowed the participants to focus on their phobic problems to reactivate their fear memory. Next, the participants were instructed that

"today"—as part of the treatment—they were going to touch a tarantula and the importance of doing this was emphasized. Participants were then instructed to directly approach an open-caged tarantula up to a distance of approximately 60 cm marked on the ground and to stay at this spot while observing the spider thoroughly. A tarantula was used because its behavior was generally predictable: the spider was always sitting at the front of the cage and rushed to the center of the terrarium when the therapist sprayed it with water. It was asked what they feared most about touching the tarantula and to what degree they expected this threat to happen on the 0- to 100-point scale(s). Next, the participants were informed that they were going to touch the tarantula, but, before doing so, they were asked to focus on their body and report their level of fear or anxiety by using the 0- to 100-point scale. After this brief 2-minute exposure to the tarantula—and without the spider being touched—the therapist closed the terrarium and the participants were seated next door, where they received (double blind) an oral dose of 40 mg of propranolol HCl or a pill placebo. Given the peak-plasma levels of propranolol HCl (38), a resting period of 90 minutes was inserted after pill administration, in which participants were offered magazines to read. After this period, blood pressures and salivary samples were again collected. See the Supplement and Table S2 for details on the physiological measurements.

Propranolol No-Reactivation. After the physiological measurements and the administration of the Structured Clinical Interview for DSM-IV (37), the participants in the propranolol no-reactivation group received (single blind) 40 mg of propranolol HCl. After a resting period of 90 minutes, the physiological measurements were again collected.

Posttreatment BAT With Tarantula (t2). Given the elimination half-life of propranolol HCl (i.e., ±5 hours) (38), testing should occur at least 24 hours later, allowing the drug to wash out; however, for logistic reasons, the first test took place 4 days after treatment. During this test, the participants were administered the tarantula BAT.

Posttreatment BAT With Baby Tarantula (t3, t4, and t5). Both the Spider Phobia Questionnaire and the baby-tarantula BAT were completed in all three sessions.

RESULTS

See the Supplement for the statistical analyses and an omnibus mixed repeated-measures analysis of variance.

A certain level of threat expectancy—which is necessary for post-retrieval plasticity (27) — was observed in both the propranolol group (mean [M] = 78.0, standard deviation [SD] = 15.6) and pill placebo group (M = 69.3, SD = 28.4) during retrieval ($F_{1,28} < 1.07$).

At pretreatment (t0), the participants in the three groups did not differ in their behavior toward the baby tarantula ($F_{2,42} < 1$), nor in their reported spider fear on the Spider Phobia Questionnaire (27) ($F_{2,42} < 1$) (Figure 2 and Figure 3).

Groups reported equal fear on the 0- to 100-point scales (t1) when standing in front of the tarantula during treatment

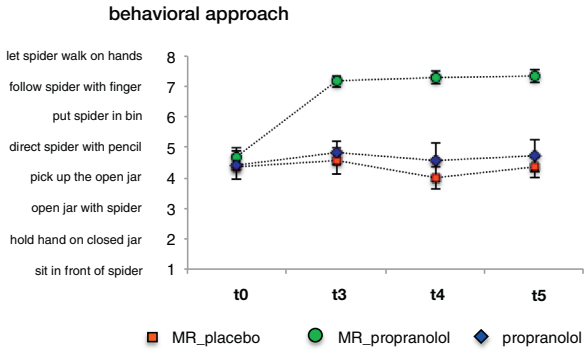

Figure 2. Behavioral approach toward the baby tarantula at t0: pretreatment and t3: posttreatment_2 as well as t4: 3-month follow-up and t5: 1-year follow-up for the three experimental groups. MR, memory reactivation.

($F_{1,28} < 1$): MR_propranolol with scores of M = 75.3 (SD = 12.6) and MR_placebo with scores of M = 80.0 (SD = 15.1).

At the first posttreatment test (t2), the participants in the MR_propranolol and MR_placebo group differed in their fear scores when standing in front of the spider (from t1 to t2) ($F_{1,28} = 4.39$, $p < .05$, $\eta^2_p = .14$). Whereas the reported fear dropped from M = 75.3 (SD = 12.6) to M = 58.9 (SD = 21.7) in the MR_propranolol group ($t_{(14)} = 2.65$, $p < .05$, two-tailed), the reported fear remained stable in the MR_placebo group (M = 79.3, SD = 12.1, $t_{(14)} < 1$) (Figure 4). Furthermore, the participants in the three groups also differed in their approach behavior toward the tarantula ($F_{2,42} = 6.99$, $p < .01$) and the associated fear scores ($F_{2,42} = 4.85$, $p < .05$). All the participants in the MR_propranolol group touched the tarantula (M = 5.0, SD = 0), whereas participants in the MR_placebo group (M = 2.9, SD = 2.1) as well as propranolol no-reactivation group (M = 3.3, SD = 1.8) barely touched its container. Follow-up analyses indeed revealed that the approach in the MR_propranolol group strongly diverged from both the MR_placebo group ($F_{1,28} = 14.72$, $p = .01$) and the propranolol no-reactivation group ($F_{1,28} = 12.32$, $p < .01$). Conversely, participants in the MR_placebo and propranolol no-reactivation group showed comparable approach behavior

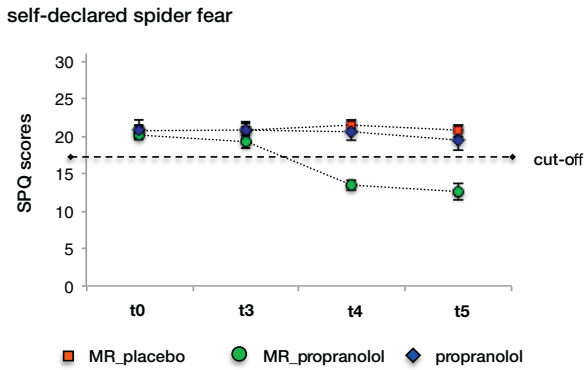

Figure 3. Self-declared spider fear on the Spider Phobia Questionnaire at t0: pretreatment and t3: posttreatment as well as t4: 3-month follow-up and t5: 1-year follow-up for the three experimental groups. MR, memory reactivation; SPQ, Spider Phobia Questionnaire.

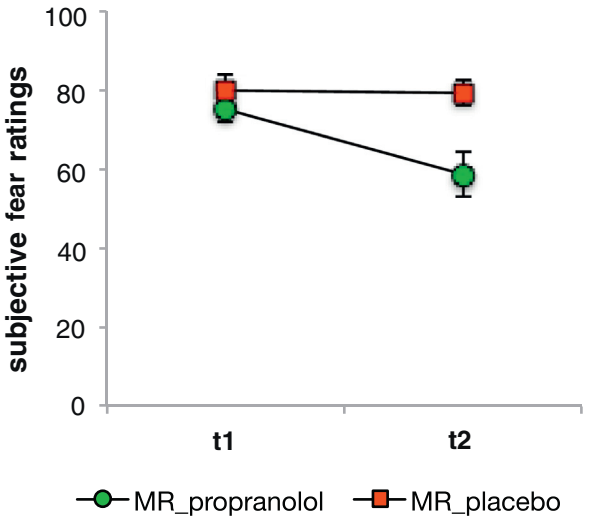

Figure 4. Self-reported fear when standing in front of the tarantula at t1 and t2 for the MR_propranolol group and the MR_placebo group. MR, memory reactivation.

($F_{1,28} < 1$). See the Supplement and Figure S1 for further details.

Participants in the three groups (t3) also differed significantly in their behavior toward the baby tarantula (t0 vs. t3, $F_{2,39} = 13.17$, $p < .001$, $\eta^2_p = .40$) (Figure 2). Participants in the MR_placebo and propranolol no-reactivation group did not progress in their approach behavior toward the baby tarantula from pretreatment (t0) to posttreatment (t3) ($F_{1,26} < 1$). The participants in the MR_propranolol group progressed from holding the jar with the baby tarantula at t0 (M = 4.7, SD = 1.3) to touching the spider or even holding it with their bare hands at t3 (M = 7.1, SD = 0.8, $t_{(13)} = 6.6$, $p < .001$, two-tailed). Indeed, this differed from the progression of the participants in both the MR_placebo group ($F_{1,25} = 19.89$, $p < .001$) and propranolol no-reactivation group ($F_{1,27} = 15.55$, $p = .001$, $\eta^2_p = .37$). See the Supplement for further details. Interestingly—despite the progression in approach behavior towards spiders in the MR_propranolol group—the self-reported degree of spider fear on the Spider Phobia Questionnaire remained unchanged at t3 in all three groups ($F_{2,39} < 1$) (Figure 3).

Remarkably, when the participants were again tested 3 months later (t4), the reported spider fear on the Spider Phobia Questionnaire significantly differed between the three groups (t3 vs. t4, $F_{2,37} = 24.78$, $p < .001$, $\eta^2_p = .57$). At 3-month follow-up, the reported spider fear had significantly decreased from t3 to t4 in the MR_propranolol group ($t_{(13)} = 5.66$, $p < .001$) compared with the MR_placebo group ($F_{1,25} = 30.82$, $p < .001$, $\eta^2_p = .55$) and propranolol no-reactivation group ($F_{1,25} = 23.01$, $p < .001$, $\eta^2_p = .48$) (Figure 3). Reported spider fear for the participants in the MR_propranolol group (M = 13.9, SD = 2.2) now fell significantly below the cut-off for the present experiment. Also, their scores are comparable to those of other spider-fearful individuals who had received 2.5 hours of exposure in vivo for their spider fear (39). However, the self-declared spider fear (i.e., SPQ) remained stable in the MR_placebo and propranolol no-reactivation group ($F_{1,24} < 3.68$). Moreover, the degree of approach behavior toward the baby tarantula persisted from t3 to t4 (i.e., 3-month follow-up) in all three groups ($F_{2,37} = 2.27$), indicating that the spider fear in the MR_propranolol group had not spontaneously recovered with time (Figure 2).

Furthermore, disrupting the process of reconsolidation by a single pill of 40 mg of propranolol persistently diminished the self-reported fear on the Spider Phobia Questionnaire, and the degree of approach behavior toward the baby tarantula remained unchanged from 3 months to 1 year follow-up (t4 to t5) in all three groups ($F_{2,32} < 1$, $F_{2,31} < 1$) (Figure 2 and Figure 3).

DISCUSSION

The current findings provide strong evidence that disrupting the process of memory reconsolidation by a noradrenergic β-blocker transferred avoidance behavior into approach behavior in individuals with spider phobia. Essential for the feasibility of reconsolidation-based interventions, the fear-reducing effect on this behavioral level (a) was not restricted to the phobic stimulus to which the participants were previously exposed (i.e., tarantula) but generalized to another spider and (b) persisted at 1-year follow-up. We cannot exclude, however, that the fear reduction was actually due to a carryover effect of the initial change in fear behavior to the original phobic stimulus at the first posttreatment assessment (t2). Even if this would be the case, the observed change in fear behavior toward both the original and novel phobic stimulus is substantial. This finding is in line with observations from our fear-conditioning studies, in which the fear erasure was not restricted to the reactivated stimulus itself but generalized to stimuli from the same semantic category (11,12).

Interestingly, the β-adrenergic drug during reconsolidation did not affect the self-declared fear on the Spider Phobia Questionnaire, but a change at this level followed the instant behavioral transformation several months later. Our finding supports laboratory studies on disrupting reconsolidation wherein propranolol solely erased the amygdala-dependent startle reflex while leaving the concomitant threat expectancy learning unaffected (10–13). Propranolol is indeed supposed to specifically act on the β-adrenergic receptors in the amygdala (15,40,41), a brain area essential for the emotional and not the cognitive expression of fear memory (42). Apparently the very short exposure to the phobic stimulus followed by a β-adrenergic drug targeted the evaluative learning component but not the expectancy learning. Although there is evidence that expectancy learning and evaluative learning may co-occur in a traditional fear-conditioning procedure (7), research on the functional properties of these forms of learning has also shown that they can be separated by experimental manipulations. One of the most important properties of evaluative conditioning is its relative resistance to extinction (43–46). To the extent that negative valence is associated with avoidance/escape action tendencies, such a residual negative valence might function as an affective-motivational source for the re-emergence of conditioned fear responses (7). Repeated observations that memory retrieval techniques—exposure to primary reinforcers (reinstatement), a change in context (renewal) or simply the passage of time (spontaneous

recovery)—did not lead to the re-emergence of fear responding as is generally observed after extinction training (10,24,47,48), suggest that disrupting reconsolidation targets the affective value of the fear memory. Yet, it seems that a reduction of fear behavior enables one to learn from disconfirming information, thereby affecting the cognitive expression of spider fear later in time. As such, the current finding challenges one of the fundamental tenets of cognitive-behavioral therapy that emphasizes changes in cognitions as central to behavioral modifications (49). Disrupting reconsolidation instead acts in a reversed order: it targets the fear behavior and subsequently the cognitions may change.

Currently cognitive-behavioral therapy is still the treatment of choice for anxiety disorders. A key ingredient of this therapy is exposure-based intervention, comprising in vivo or imaginary confrontations with the feared object without any adverse consequences. Such extinction-like exposure treatments teach the patient that the feared stimulus is innocuous but do not alter original fear memories (48,50). Extinction solely involves the formation of a new inhibitory memory trace that competes with the original fear memory (51,52). Without keeping this new memory alive through practicing the learned behavior, the intact amygdalar-dependent fear memories may always resurface resulting in a partial or full reappearance of fear. Notwithstanding the success of exposure-based treatments for anxiety disorders, a substantial proportion of patients still have a relapse of fear after successful treatment (53,54).

One way to counteract the return of fear is by identifying therapeutic strategies for enhancing inhibitory learning; this form of learning forms the basis of cognitive behavioral treatment for fear and anxiety disorders (55). A number of so-called cognitive enhancers have been uncovered, including yohimbine, which increases central noradrenergic transmission or D-cycloserine, a partial agonist at the glycine site of *N*-methyl-D-aspartate glutamate receptors (56,57). Even though the discovery of cognitive enhancers may be promising by accelerating treatment effectiveness, they do not prevent the return of fear because they leave the fear memory intact. Here, we present a fundamentally alternative strategy in which the pharmacological intervention on memory retrieval weakens the fear memory itself. Hence, the (re)discovery that fear memory is not necessarily permanent but can be eliminated when retrieved may be a promising alternative for clinical practice. It not only realizes the reduction of fear within a few minutes but it may also solve the problem of relapse. Yet, in considering clinical applications, several issues must be addressed in future research. First, the present experiment was conducted in a sub-clinical population of spider-fearful individuals, and an important question to be answered is whether a similar protocol will be as successful in patient populations. Second, it remains unclear which distinctive features of the retrieval session triggered the process of reconsolidation in the current setting. In fear-conditioning studies, the successful engagement of the process of memory reconsolidation by retrieval requires a "violation of expectations," or a mismatch, between what occurs and what was expected according to the original CS–US association, often now referred to as a prediction error (13,58). In the current study, it remains unclear what exactly triggered the memory destabilization. The spider-fearful participants were instructed to touch the spider, but in reality this never happened to prevent possible extinction learning. Given that a phobic stimulus usually triggers avoidance behavior, the tendency to approach the spider might have been sufficient to destabilize the fear memory. Because minor environmental changes define whether memory retrieval induces memory reconsolidation (29,30), future research should delineate the optimal and boundary conditions to trigger memory reconsolidation in clinical settings. Although further insights on prediction error is required for the success of reconsolidation-based interventions, a new wave of treatments that pharmacologically target the underlying processes of learning and memory seems to be within reach.

ACKNOWLEDGMENTS AND DISCLOSURE

This work was supported by a VICI-grant (MK) from the Netherlands Organization for Scientific Research. We sincerely thank Wouter Cox and Norah Schulten for assisting with the data collection and Jos Bosch for saliva analysis.

The authors report no biomedical financial interests or potential conflicts of interest.

ARTICLE INFORMATION

From the Department of Clinical Psychology, University of Amsterdam, Amsterdam, The Netherlands and Amsterdam Brain and Cognition, University of Amsterdam, Amsterdam, The Netherlands.

Address correspondence to Merel Kindt, University of Amsterdam, Faculty of Social and Behavioral Sciences, Department of Clinical Psychology, Weesperplein 4, 1018 XA Amsterdam, The Netherlands; E-mail: m.kindt@uva.nl.

Received Oct 6, 2014; revised Mar 18, 2015; accepted Apr 2, 2015.

Supplementary material cited in this article is available online at http://dx.doi.org/10.1016/j.biopsych.2015.04.006.

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