Psychoneuroendocrinology (2014) 41, 89—96

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Exposure to stress attenuates fear retrieval in healthy men

Christian J. Merz [1,*], Tanja C. Hamacher-Dang [1], Oliver T. Wolf

Institute of Cognitive Neuroscience, Department of Cognitive Psychology, Ruhr-University Bochum, Universitätsstr. 150, 44780 Bochum, Germany

Received 4 November 2013; received in revised form 22 November 2013; accepted 11 December 2013

KEYWORDS
Cortisol;
Extinction;
Fear conditioning;
Memory;
Socially Evaluated Cold Pressor Test;
Stress hormones

Summary The stress hormone cortisol reduces retrieval of emotional memories, which has been suggested to support the treatment of psychiatric disorders characterized by exaggerated fear-related memories. Indeed, studies in patients with anxiety disorders have indicated that the success of exposure therapy can be enhanced with accompanying cortisol administration. Fear renewal refers to the clinically relevant phenomenon that successfully extinguished fear can return after a context change. It remains to be investigated whether the effects of stress hormones on fear retrieval also generalize across different contexts. Healthy men were exposed to a fear renewal design with fear acquisition in context A and extinction in context B. Pictures of rooms served as contexts, coloured lights were introduced as conditioned stimuli (CS), and an electrical stimulation served as the unconditioned stimulus (UCS). On the next day, participants were randomly assigned to a stress (Socially Evaluated Cold Pressor Test) or a control condition (n = 20 each). We tested for fear retrieval in contexts A and B during peak cortisol concentrations after stress induction. Overall, a context × stress interaction occurred, revealing that stress attenuated skin conductance responses in the extinction context B. Stress also reduced UCS expectancy in context B. Additionally, stress abolished the renewal effect (differentiation between CS in context A) at the electrodermal level. These results demonstrate a decreased return of fear after acute exposure to stress. Stress interferes with the retrieval of the original fear memory which in turn affects extinction responding. Thus, acute stress reduces rather than promotes the return of fear.

1. Introduction

Exaggerated retrieval of anxiety-related material leads to emotional disturbances in the case of pathological fear. Clinical observations suggest that a stressful situation might evoke or boost the return of fear (Jacobs and Nadel, 1985). Treatment strategies attempt to attenuate these maladaptive processes. For example, the stress hormone cortisol was administered prior to exposure therapy in patients with anxiety disorder (de Quervain et al., 2011; Soravia et al., 2006). Indeed, cortisol successfully reduced phobic fear, which points to its potential for augmenting extinction-based therapeutical strategies. Controversially, stress sometimes appears to increase fear while at other times it relieves fear.

* Corresponding author. Tel.: +49 234 3224498; fax: +49 234 14308.
E-mail address: Christian.J.Merz@rub.de (C.J. Merz).
[1] These authors contributed equally to this work.

0306-4530/$ — see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.psyneuen.2013.12.009

Basic research is needed to integrate these seemingly opposing findings.

Strong evidence from the literature on episodic memory (for reviews: Schwabe et al., 2010; Wolf, 2009) indicates that cortisol impairs memory retrieval, but facilitates memory consolidation, in particular concerning emotional material. When exposed to phobic stimuli, patients retrieve their aversive memories. It has been suggested that cortisol may enhance extinction-based psychotherapy via two mechanisms (Bentz et al., 2010; de Quervain and Margraf, 2008): by weakening the retrieval of aversive memories and by enhancing the consolidation of the corrective experience made during exposure therapy (i.e., enhancing the consolidation of extinction memory). Apart from patient studies, a recent experiment has indicated that acute stress prior to extinction decreases fear retrieval in healthy men (Bentz et al., 2013). Altogether, the opposing effects of cortisol on different memory phases are a promising phenomenon which may be utilized in the optimization of exposure treatment.

Critically, exposure relies on extinction (Graham and Milad, 2011) which brings with it the disadvantage of context-dependency (Bouton, 2004). Thus, when patients encounter their feared objects in a context that is different from the extinction context, phobic fear often returns. The phenomenon of recovery of the extinguished (fear) response in a context different from the extinction context is termed renewal (Bouton, 2004). It remains to be seen whether cortisol, besides alleviating fear retrieval in the extinction context, also shows a corresponding generalized effect in another context. In this framework, the original context in which fear was acquired constitutes the most fearful context. Successful treatment should reduce the fear response not only in the extinction context, but also in the powerful acquisition context, thus decreasing fear renewal.

In the present study, healthy men were subjected to a typical fear renewal design (cf. Milad et al., 2007, 2009) with fear acquisition in context A and extinction in context B. On the next day, they were either exposed to stress or a control condition. During peak cortisol concentrations the fear retrieval test was conducted in context A (to test for stress effects on fear renewal) and B (to investigate the influence of stress on fear extinction memory). Based on preliminary evidence that pre-extinction stress might reduce the retrieval of fear memory (Bentz et al., 2013) and in line with assumptions regarding the underlying mechanisms of cortisol enhancement in psychotherapy (Bentz et al., 2010; de Quervain and Margraf, 2008), we expect that stress will impair the retrieval of conditioned fear. This effect may be modulated by context, as has been observed for stress effects on episodic memory retrieval (Schwabe and Wolf, 2009).

2. Materials and methods

2.1. Participants

Forty healthy male students recruited at the Ruhr-University Bochum participated in this study and were randomized to two experimental groups (stress vs. control; Section 2.4). Compliance with inclusion criteria was checked beforehand in a standardized telephone interview; students reporting chronic or acute illnesses, colour blindness, regular intake of medicine, current medical or psychological treatment, drug use including smoking, body mass index (BMI) $<18\ kg/m^2$ or $>27\ kg/m^2$, age <18 years or >40 years were not eligible for participation.

During the two-day testing period, participants were advised not to drink alcohol and to refrain from exhausting physical exercise. In addition, they were instructed not to consume food or drinks except water and not to do any physical exercise 90 min before the start of the session on day 2. At the end of the second testing session, participants were reimbursed with 25€ for their participation and received additional information regarding the aim of the study. All procedures were in accordance with the Declaration of Helsinki and approved by the university's local ethical review board.

2.2. Stimulus material

The stimulus material was presented using Presentation (Neurobehavioral Systems) on a 19-inch computer screen located approximately 50 cm in front of the participants. All stimuli and the entire procedure were adopted from Milad and colleagues (2007, 2009). Pictures of an office room and a room with a shelf served as contexts A and B, respectively. Each of the contexts included a desk lamp for presentation of the conditioned stimuli (CS). The lamp switched on after 3 s of context presentation, shining either in red, blue or yellow for 6 s.

A pseudo-randomized stimulus order was used in which no more than two consecutive presentations of the same CS were allowed. Allocation of the three colours of light (red, blue, yellow) as CS+ and CS− as well as order of context and CS presentations on day 2 were counterbalanced between participants. On day 2, the six possible combinations of CS and contexts were presented in pseudo-randomized orders with the additional restriction that all six combinations have to occur once during the first six trials. A black screen with a white fixation cross was shown during the inter-trial intervals between the end of a CS presentation and the start of the next context presentation, randomly set between 6 s and 8 s.

A constant voltage stimulator (STM200; BIOPAC Systems, Inc.) provided transcutaneous electrical stimulation (100 ms) via two Ag/AgCl electrodes filled with isotonic electrolyte medium (Synapse Conductive Electrode Cream, Kustomer Kinetics Inc., Arcadia, CA) fixed to the middle of the left shin. Intensity was set individually to "unpleasant but not painful" using a gradually increasing rating procedure. The electrical stimulation was used as unconditioned stimulus (UCS) occurring immediately after CS+ offset (delay conditioning; 62.5% partial reinforcement rate).

2.3. Fear conditioning, extinction, and retrieval procedure

After arrival, participants were given a resting phase of 20 min in which they provided written informed consent, filled out questionnaires on demographic variables and were tested for red-green colour blindness using five Ishihara plates (selected from Ishihara, 1990). Furthermore, they were informed about the course of the experiment (SCR measurement, application of electrical stimulation, stress, saliva sampling) and given the possibility to ask questions.