



Endogenous cortisol levels influence exposure therapy in spider phobia



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ARTICLE INFO

Article history:

Received 21 October 2013

Received in revised form

26 June 2014

Accepted 30 June 2014

Available online 8 July 2014

Keywords:

Cortisol

Glucocorticoids

Exposure therapy

Spider phobia

Anxiety disorders

Extinction learning

ABSTRACT

Previous research in patients with phobia showed that the administration of glucocorticoids reduces fear in phobic situations and enhances exposure therapy. Glucocorticoids underlie a daily cycle with a peak in the morning and low levels during the evening and night. The aim of the present study was to investigate whether exposure is more effective when conducted in the morning when endogenous cortisol levels are high. Sixty patients meeting DSM IV criteria for specific phobia (animal type) were randomly assigned to one-session exposure treatment either at 08.00 a.m. (high cortisol group) or at 06.00 p.m. (low cortisol group). Participants returned for a posttreatment assessment one week after therapy and a follow-up assessment three months after therapy. Both groups showed good outcome, but patients treated in the morning exhibited significantly less fear of spiders in the behavioral approach test (BAT) and a trend for lower scores on the Fear of Spiders Questionnaire (FSQ) than patients treated in the evening. This effect was present at posttreatment and follow-up. Our findings indicate that exposure therapy is more effective in the morning than in the evening. We suggest that this may be due to higher endogenous cortisol levels in the morning group that enhance extinction memory.

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Introduction

Specific phobias are among the most common anxiety disorders with an estimated lifetime prevalence of 12.5% (Michael, Zetsche, & Margraf, 2007). They are characterized by marked and persistent fear that is excessive and unreasonable, cued by the presence or anticipation of a specific object or situation. A central mechanism in the pathogenesis of phobic disorders is associative learning or conditioning that leads to the formation of fear memory (Field, 2006; Michael & Ehlers, 2009; Michael, Munsch, & Margraf, 2009; Mineka & Oehlberg, 2008). Exposure to feared objects or situations is the treatment of choice for anxiety disorders (Choy, Fyer, & Lipsitz, 2007; Hofmann & Smits, 2008; Norton & Price, 2007). Exposure therapy is thought to rely on the extinction of the fear memory. Thus, exposure therapy is best conceptualized as a learning process in which new non-fear memory traces are established, which inhibit the old fear memories (Hermans, Craske, Mineka, & Lovibond, 2006).

Even though exposure therapy is a highly successful treatment option, not all patients profit from it (Choy et al., 2007). Recently, several pharmacological agents have been proposed as boosters of exposure therapy (Bentz, Michael, de Quervain, & Wilhelm, 2010; Vervliet, 2008). These new therapeutic approaches are based on the idea that the pharmacological agents facilitate the learning processes underlying the success of exposure therapy (Hofmann, Pollack, & Otto, 2006; Otto, Basden, Leyro, McHugh, & Hofmann, 2007; Rabinak et al., 2013). One agent that has been suggested to improve exposure therapy is cortisol. There is growing evidence from studies in humans and animals that cortisol has the potential to facilitate the processes leading to an enhanced extinction learning during exposure therapy. In detail, cortisol has been shown to enhance the consolidation of newly acquired material and inhibit the retrieval of previously learned material (for a review see de Quervain, Aerni, Schelling, & Roozendaal, 2009). This characteristic of cortisol makes it a promising tool to enhance exposure therapy for anxiety disorders, in which the retrieval of previously learned anxiety related material (e.g. spider is a dangerous animal that wants to harm me) should be inhibited and the consolidation of the newly learned corrective experiences (e.g. spider is not dangerous and does not do any harm) should be enhanced (Bentz et al., 2010). Two recent studies in patients found evidence that exogenous cortisol administration prior to exposure with feared

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stimuli or situations leads to a greater anxiety reduction than exposure without cortisol administration (Soravia et al., 2006). Cortisol was administered to 20 spider phobia patients and 40 social phobia patients in a double-blind placebo-controlled design. In the spider phobia study, repeated oral administration of cortisol (10 mg) 1 h before exposure to spider photographs induced a progressive reduction of stimulus-induced fear. In the social phobia study cortisol administered prior to a socially evaluative stressor reduced fear during the anticipation, exposure and recovery phase of the stressor.

Based on these findings de Quervain and colleagues investigated the effects of cortisol administration on exposure therapy in height phobia. In a double-blind placebo-controlled study, 40 patients with specific phobia for heights were treated with three sessions of exposure therapy using virtual reality exposure to heights. Cortisol (20 mg) or placebo was administered orally 1 h before each of the treatment sessions. Adding cortisol to exposure therapy resulted in a significantly greater reduction in fear of heights both at post-treatment and at follow-up (de Quervain et al., 2011). Thus, there is evidence that exposure therapy which is combined with exogenous cortisol administration is more effective than exposure therapy without cortisol administration.

Cortisol is secreted as a response to stress and can be administered exogenously. However, cortisol secretion also underlies a daily cycle with a peak in the morning and low levels during the evening and night (Kirschbaum & Hellhammer, 1989). Several studies have shown that these endogenous variations in cortisol level also influence learning and memory processes (Preuss, Schoofs, & Wolf, 2009; Putman, Van Honk, Kessels, Mulder, & Koppeschaar, 2004; Van Honk et al., 2003). Thus, the aim of the present study was to investigate whether these diurnal variations in endogenous cortisol levels can be utilized for optimizing the effect of exposure therapy. In our study, sixty patients meeting DSM-IV criteria for specific phobia (animal type) were randomly assigned to receive three hours exposure treatment for spider phobia delivered in a single therapy session (as described by Ost, 1989) either at 08.00 a.m. (high cortisol group) or at 06.00 p.m. (low cortisol group). Patients returned for a posttreatment assessment one week after therapy and a follow-up assessment three months after therapy. The reduction in fear of spiders was measured with a behavioral approach test (BAT) and with the German version of the Fear of Spiders Questionnaire (FSQ, Szymanski & O'Donohue, 1995). Based on previous findings on exogenous cortisol administration (de Quervain et al., 2011; Soravia et al., 2006; Suris, North, Adinoff, Powell, & Greene, 2010), we predicted that patients who were treated in the morning (when endogenous cortisol levels are high) show greater reduction in fear of spiders as measured by the BAT and the FSQ as patients treated in the evening (when endogenous cortisol levels are low).

Methods and materials

Patients' characteristics

Patients aged 18–50 with spider phobia were recruited via newspaper advertisements and flyers posted at the Saarland University and health institutions. A total of 109 patients responded and, after a telephone screening, 69 patients were invited for a pretreatment interview.

Participation was restricted to healthy, non-smoking women using oral contraceptives with a body mass index between 20 and 25. Furthermore, patients with a recent history of systemic or oral cortisol therapy and who were pregnant or lactating were excluded from analysis. These stringent exclusion criteria were applied, because basal cortisol levels are known to be influenced by these

factors. Furthermore, we excluded patients with any axis I disorder (other than spider phobia), severe acute or chronic disease (e.g. lung or heart diseases), allergic reactions to insect bites, and current pharmacological treatment or psychotherapy.

We also required patients to refrain from physical exercise, alcohol and caffeinated drinks (factors known to influence cortisol levels) within 3 h prior to therapy. 60 participants fulfilled the inclusion criteria. All participants gave their written informed consent. The research was approved by the ethical committee of the medical association of Saarland.

Procedure and design

The study took place at the psychotherapy outpatient unit of the Department of Clinical Psychology and Psychotherapy of the Saarland University. Participation included four appointments: an initial screening session clarifying study eligibility and assessing symptoms (pretreatment assessment), a three-hour-treatment session, an assessment one week after treatment (posttreatment assessment), and a follow-up assessment 12–14 weeks after treatment (follow-up assessment).

Patients were randomized by an independent person to either treatment in the morning or treatment in the evening.

The treatment followed strictly Ost's manual for specific phobias (Ost, 1989). Therapists were trained by Lars-Göran Öst, regular supervision was provided by experienced psychotherapists of the psychotherapy outpatient unit of the Department of Clinical Psychology and Psychotherapy of Saarland University. Before the study started, all therapists had completed at least three video-recorded pilot treatments. During therapy patients were gradually exposed to spiders. Only spiders indigenous to Germany were used (ranging in size from 1 cm to approximately 5 cm), and three jars with spiders of increasing size were prepared.

Pretreatment interview

Patients who volunteered to participate in the study were contacted by phone for a short screening interview. If patients fulfilled inclusion criteria, the experimenter scheduled a date for the pretreatment interview. The interview lasted approximately 60 min. To diagnose Specific Phobia (animal type) and exclude any other Axis I disorder we conducted a structured interview (modified German version of the ADIS-IV (MINI-DIPS, Margraf, 1994). After checking inclusion and exclusion criteria, the BAT was conducted and patients completed the FSQ (Szymanski & O'Donohue, 1995) and several other questionnaires assessing control variables (Becks Depression Inventory (BDI) Hautzinger, Bailer, Wollar, & Keller, 1995) (State Trait Anxiety Inventory (STAI) Laux, Glanzmann, Schaffner, & Spielberger, 1981), (Morningness-Eveningness-Questionnaire (MEQ) Horne & Ostberg, 1976)).

Additionally, cortisol levels from hair and saliva were collected as control variables in order to determine the basal cortisol status of the patients. After patients had completed the questionnaires, the therapist took a small hair sample from each participant in order to determine the long-term cortisol levels of each participant. Patients were further instructed to provide 5 saliva samples on two consecutive mornings prior to the therapy session in order to determine the cortisol awakening reaction. They collected one saliva sample directly after awakening and four more at 15, 30, 45 and 60 min after awakening. After receiving these instructions an appointment for the therapy session was made.

Therapy session

Patients arrived for therapy at 08.00 a.m. or at 06.00 p.m. The therapist welcomed the patient, collected the saliva samples from the participant, and asked her to fill out the Positive and Negative

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