



Dispositional cognitive reappraisal modulates the neural correlates of fear acquisition and extinction



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ABSTRACT

Adverse learning experiences play a significant role in the etiology of anxiety disorders. However, not all individuals experiencing negative events develop heightened anxiety. This is possibly due to individual differences in the regulation of negative emotions associated with these negative events. Cognitive reappraisal is defined as reinterpreting an emotion-eliciting situation in a way that changes its emotional impact. A more frequent use of cognitive reappraisal in daily life has been shown to be more adaptive. However, no study to date examined the association of dispositional cognitive reappraisal with emotional learning, in order to elucidate individual differences in negative emotional responses towards aversive events.

The goal of this functional magnetic resonance imaging (fMRI) study was to investigate the association of dispositional cognitive reappraisal with subjective, electrodermal and neural correlates of fear acquisition and extinction. Data of 41 healthy individuals, who participated in a socially relevant differential conditioning paradigm (acquisition and extinction learning: day 1, extinction recall: day 2), were acquired.

Dispositional cognitive reappraisal was negatively associated with right insula, and hippocampus activation during acquisition. Furthermore, the reduction of self-reported conditioned fear during extinction learning as well as reduced insula and enhanced rostral anterior cingulate cortex activation during extinction learning was related to cognitive reappraisal. In addition, reduced recovery of conditioned arousal, reduced anterior cingulate and dorsomedial prefrontal cortex activation and enhanced ventromedial prefrontal cortex activation during extinction recall was observed in individuals with higher cognitive reappraisal scores.

The results indicate that dispositional cognitive reappraisal modulates subjective and neural correlates of fear conditioning, probably leading to reduced acquisition and stronger extinction learning and recall. These results point to the important role of dispositional cognitive reappraisal in the development and modification of conditioned emotional responses and might further improve our understanding of anxiety disorders.

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1. Introduction

Emotional learning processes as for instance fear conditioning are assumed to be important mechanisms in the etiology of anxiety disorders (Mineka & Oehlberg, 2008), possibly leading to the development of (pathological) anxiety in response to negative events or traumata. Previous fear conditioning studies showed an involvement of several brain structures as the amygdala, insula, hippocampus and dorsal anterior cingulate cortex (dACC) in the acquisition of fear responses (for an overview see Etkin & Wager, 2007; Sehlmeier

et al., 2009). Besides stronger acquisition of fear responses, dysfunctional extinction learning and recall are supposed to be further important factors in the etiology and maintenance of anxiety disorders (Graham & Milad, 2011). Especially the amygdala and the ventromedial prefrontal cortex (vmPFC) are assumed to be critical brain structures for extinction learning and the vmPFC and hippocampus for the recall of extinction (Diekhof, Geier, Falkai, & Gruber, 2011; Kalisch et al., 2006; Milad et al., 2007; Phelps, Delgado, Nearing, & LeDoux, 2004; Sehlmeier et al., 2009). Stronger amygdala activation during extinction learning and dysfunctional reduced activation of the vmPFC and hippocampus along with dACC hyperactivation has been observed in posttraumatic stress disorder (PTSD) patients during the recall of extinction (Milad et al., 2009).

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However, not all individuals experiencing negative life events or traumata develop exaggerated anxiety or even anxiety disorders. This points to the involvement of further moderating factors, as for instance the ability to regulate one's own negative emotions in stressful situations. Cognitive reappraisal, one form of cognitive emotion regulation, is defined as interpreting a potentially emotion-eliciting situation in a way that changes its emotional impact (Gross & John, 2003). Cognitive reappraisal has been shown to be an adaptive emotion regulation strategy, and people differ in the extent they typically use cognitive reappraisal in order to regulate their emotions in daily life (dispositional cognitive reappraisal). A higher dispositional use of cognitive reappraisal is associated with better interpersonal functioning, enhanced well-being, and reduced depressive symptoms (Gross & John, 2003). Functional imaging studies indicate an association of dispositional reappraisal with reduced amygdala activation during emotional face processing (Drabant, McRae, Manuck, Hariri, & Gross, 2009), stronger dACC and dorsolateral prefrontal cortex responses during response inhibition towards negative emotional material (sad vs. happy faces; Vanderhasselt, Baeken, van Schuerbeek, Luypaert, & de Raedt, 2013), and stronger down-regulation of amygdala activation during instructed emotion regulation in a group of patients with remitted depression and healthy controls (Kanske, Heissler, Schönfelder, & Wessa, 2012). Structural imaging studies reported an association of habitual cognitive reappraisal with larger dACC (Giuliani, Drabant, & Gross, 2011), amygdala (Hermann, Bieher, Keck, Vaitl, & Stark, *in press*), and vmPFC volumes (Welborn et al., 2009), brain regions that are also functionally involved in the cognitive regulation of emotions (for an overview see Ochsner & Gross, 2005). There is only one fMRI study (Delgado, Nearing, Ledoux, & Phelps, 2008) showing a reduction of conditioned responding in the amygdala through direct emotion regulation (via imagining something calming in nature) during an instructed fear conditioning paradigm. Interestingly, one further study found a negative association of dispositional reappraisal and right anterior insula activation during the anticipation of aversive images (Carlson & Mujica-Parodi, 2010), indicating the importance of trait differences in the habitual use of cognitive reappraisal in the handling of upcoming aversive situations. In another study, we have furthermore shown that higher dispositional cognitive reappraisal was associated with reduced activation decline in the vmPFC over the course of symptom provocation in specific phobia (Hermann et al., 2013). However, no study up to date investigated the association of individual differences in cognitive reappraisal usage and neural correlates during the acquisition and extinction of conditioned responses.

The aim of this functional magnetic resonance imaging (fMRI) study was therefore to investigate the association of dispositional cognitive reappraisal and subjective, electrodermal and neural conditioned responses in a social conditioning paradigm. The goal of this study was to investigate conditioning processes, which are relevant in daily life and might contribute to the development and maintenance of anxiety disorders. Therefore, we used a social conditioning paradigm, which seems to meet these requirements, but is also comparable to classical fear conditioning designs. A previous social conditioning study found enhanced activation of different amygdala subregions during learning of affective values of faces (Davis, Johnstone, Mazzulla, Oler, & Whalen, 2010). Furthermore, instructed and observational fear learning, other forms of social learning, have been shown similar results concerning enhanced conditioned skin conductance responses and amygdala activation compared with classical fear conditioning (Olsson, Nearing, & Phelps, 2007; Olsson & Phelps, 2004). Additionally, social conditioning has the further advantage that it might involve more cognitive processes compared with traditional fear conditioning paradigms. These might be modifiable more easily with

cognitive reappraisal strategies and subsequently lead to a stronger impact of individual differences in dispositional cognitive reappraisal on associative learning processes.

Forty-one individuals participated in a two-day differential social conditioning paradigm with acquisition and extinction learning on the first and extinction recall on the second day. Neutral facial stimuli of two women and two men served as conditioned stimuli (CS), whereas short film clips with (spoken) critical/insulting comments of these two women and men were used as UCS. The main results of this social conditioning study as well as the correlation of social anxiety with subjective, electrodermal and neural conditioned responses have been reported elsewhere (Pejic, Hermann, Vaitl, & Stark, 2013). In short, conditioned responses appeared in the left amygdala, left hippocampus and right dACC during acquisition, whereas extinction was characterized by activation in bilateral amygdala and hippocampus. Subjective responses indicated successful acquisition and extinction, whereas no significant conditioned skin conductance responses appeared. Social anxiety was correlated with enhanced amygdala and hippocampal activation during acquisition, reduced responses in these brain regions during extinction learning, and reduced activation of the vmPFC during extinction recall.

The goal of the actual study was to evaluate the relationship between dispositional reappraisal and subjective, electrodermal and neural conditioned responses in this social conditioning paradigm. Less frequent use of reappraisal was expected to correlate with a stronger and more exaggerated acquisition of fear responses as well as with reduced extinction learning and extinction recall.

2. Material and methods

2.1. Subjects and questionnaires

Forty-nine healthy individuals (23 females, 26 males) participated in a socially relevant differential conditioning fMRI study (acquisition and extinction learning: day 1; extinction recall: day 2). This study is part of a larger study investigating the neural basis of emotional learning and regulation processes and was approved by the ethics committee of the German Psychological Society. The main results of this study and the association with social anxiety have been published elsewhere (Pejic et al., 2013). Exclusion criteria consisted of medical, neurological, and psychiatric diseases, MRI contraindications, or use of psychoactive or other potentially confounding drugs or medications. Most participants were students; all of them were right-handed. They gave written informed consent in accordance with the guidelines of the ethical standards of the Declaration of Helsinki. Eight subjects were excluded due to several reasons (head movements during scanning, technical problems with the stimulus presentation, early termination of the experiment, one subject fell asleep and one was excluded due to an outlier score (>2 SDs above the mean) in a measure of social anxiety (Social Phobia Inventory; SPIN; Sosic, Gielert, & Stangier, 2008)), leaving 41 subjects (19 males, 22 females; age: $M = 23.49$ years, $SD = 3.075$ years, range: 19–32 years) for final analysis.

All subjects completed the emotion regulation questionnaire (Gross & John, 2003; German version: Abler & Kessler, 2009) to assess the habitual use of reappraisal (as the interesting variable in this study) and expressive suppression (a more response-focused emotion regulation strategy). The participants had to answer 10 items (example item of the reappraisal scale: "When I want to feel less negative emotion, I change the way I'm thinking about the situation.") on a 7-point scale (1 = "strongly disagree", 4 = "neutral", 7 = "strongly agree"). For the purpose of this study, the mean score of the six reappraisal items was calculated

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