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No effect of trait anxiety on differential fear conditioning or fear generalization

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ABSTRACT

Previous studies have shown that individuals with anxiety disorders exhibit deficits in fear inhibition and excessive generalization of fear, but little data exist on individuals at risk from these disorders. The present study examined the role of trait anxiety in the acquisition and generalization of fear in 126 healthy participants selected on the basis of their trait-anxiety scores. Measures of conditioning included fear-potentiated startle, skin conductance response and online risk ratings for the unconditioned stimulus. Contrary to our hypotheses, trait anxiety did not have any effect either on the acquisition or the generalization of fear. Our results suggest that these fear conditioning processes are not impaired in individuals at risk from anxiety.

1. Introduction

Fear conditioning is a form of associative learning by which a neutral stimulus becomes a conditioned stimulus (CS) that elicits a fear response after being paired with an innately aversive stimulus (unconditioned stimulus, US). This process allows the organism to respond appropriately to stimuli that signal a potential threat. However, when fear is expressed in non-threatening situations, such as in anxiety disorders, it becomes pathological.

Fear conditioning has been widely studied as a source of individual differences in the pathogenesis of anxiety. In a recent quantitative meta-analysis, Lissek et al. (2005) reviewed 20 empirical studies that compared patients with anxiety disorders and healthy individuals with regard to fear conditioning. The studies reviewed used either a simple or a differential conditioning paradigm. In the former, a single CS is paired with the US (CS+), whereas in the latter, a CS is paired with the US (CS+) and another CS is presented in the absence of the US, thus becoming a safety signal (CS−). Relative to healthy individuals, anxious patients displayed stronger fear responses to the CS+ in simple conditioning studies. They also showed increased fear both to the CS+ and the CS− in studies using differential conditioning. In addition, anxious patients displayed stronger fear responses during extinction (the phase following acquisition in a typical fear conditioning experiment, when the CS is no longer followed by the US).

These difficulties in suppressing fear responses to the CS− during acquisition and to the CS+ during extinction may be taken as evidence of deficits in fear inhibition processes among anxious patients (Davis et al., 2000). Recent studies (not included in the aforementioned meta-analysis) have also provided evidence consistent with deficits in fear inhibition to the CS− in patients with posttraumatic stress disorder (PTSD; Jovanovic et al., 2009, 2010) and panic disorder (Lissek et al., 2009).

The difficulties in suppressing fear responses to the CS− observed among anxious patients have also been related to the generalization of fear (Craske et al., 2009; Jovanovic et al., 2010; Lissek et al., 2005, 2009). Generalization of conditioned fear is also an adaptive process by which learned fear transfers to novel stimuli that are similar to the original CS. As in a differential conditioning paradigm, the CS+ and the CS− share many perceptual characteristics, anxious individuals would tend to transfer fear from one stimulus to the other. In fact, an excessive fear generalization (e.g., expression of fear to stimuli that resemble those present during a traumatic event or a first panic attack) may be characteristic of certain anxiety disorders (American Psychiatric Association, 2000). In the only study conducted on this topic in a clinical sample thus far, Lissek et al. (2010) found that individuals with

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panic disorder displayed greater fear generalization than healthy controls.

Most studies on individual differences in fear conditioning have been conducted in clinical samples. However, this research strategy has some limitations. First, results may be contaminated by the frequent comorbidity of different anxiety disorders, and of anxiety disorders and other psychiatric conditions (Merikangas & Swanson, 2010). Second, patients with anxiety disorders often follow pharmacological treatments that may interfere with measures of fear conditioning (e.g., Grillon & Baas, 2003) or with the conditioning process itself (Kindt et al., 2009). An alternative to circumvent these limitations is to study fear conditioning in individuals who are at risk from anxiety but do not suffer from a clinically defined anxiety disorder.

Elevated trait anxiety is an important risk factor for anxiety disorders (Chambers et al., 2004; Hettema et al., 2006). However, few studies have aimed to examine individual differences in fear conditioning as a function of trait anxiety. Consistent with the above-mentioned studies in clinical samples, Grillon and Ameli (2001) found deficits in fear inhibition in the presence of safety signals among individuals with high trait anxiety, although the goal of this study was to develop a paradigm to study conditioned inhibition, and the sample size was rather small (only 18 participants were highly anxious individuals). In addition, two recent neuroimaging studies found a significant positive association between trait anxiety and the activation of brain areas that mediated the expression of conditioned fear (Dunsmoor et al., 2011; Indovina et al., 2011).

In the present study, we examined the role of trait anxiety in the acquisition and generalization of fear. Based on previous research, we predicted that individuals with high trait anxiety would show deficits in fear inhibition (i.e., inability to suppress fear responses to CS− in a differential conditioning paradigm). We also predicted that individuals with high trait anxiety would generalize conditioned fear to a greater extent than non-anxious individuals (i.e., would show a more gradual decline in conditioned fear when stimuli ranging in perceptual similarity to the CS+ were presented). We used fear-potentiated startle (FPS), skin conductance response (SCR), and online ratings of risk for US, as measures of fear conditioning.

2. Method

2.1. Participants

Nine-hundred and ninety-two undergraduates were screened with the trait scale of the State-Trait Anxiety Inventory (STAI-T, Spanish version; Spielberger et al., 1982). The final sample consisted of 126 individuals selected on the basis of their mean trait anxiety score on two separate administrations of the STAI-T (separated by a period of 10 months on average). Three groups were thus formed (low anxiety: percentiles 1–20; medium anxiety: percentiles 36–65; and high anxiety: percentiles 81–100). Participants were screened for exclusion criteria (lifetime/current drug abuse or dependence, smoking more than 10 cigarettes per day, current psychiatric or medical disorder, pregnancy, visual/auditory impairment, and current use of medication, as per self-report) with an ad hoc structured interview conducted by a research psychologist. They were asked to abstain from alcohol, tobacco, and any other drug 24 h before the experiment, and of caffeinated drinks 12 h before the experiment. Table 1 shows the basic characteristics of each group.

The study was approved by the university ethics committee, and participants received 15€ in exchange for their time.

Table 1
Participants' characteristics and variables related to the experimental procedure (unless otherwise indicated, means and standard deviations are provided).

	Low ($n = 39$)	Medium ($n = 47$)	High ($n = 40$)
Male sex, n (%)	10 (26%)	12 (26%)	12 (30%)
Age (years)	22.77 (2.71)	21.96 (2.22)	22.26 (2.74)
STAI-T[a]	8.41 (2.30)	20.11 (1.99)	37.92 (4.08)
Contingency-unaware individuals[b], n (%)	4 (10%)	7 (15%)	4 (10%)
Shock intensity (mA)[c]	3.68 (0.18)	3.57 (0.14)	3.31 (0.13)
Shock discomfort (1–10)[c]	6.41 (0.23)	6.57 (0.25)	6.93 (0.22)
Startle probe discomfort (1–10)[c]	7.13 (0.28)	6.70 (0.28)	7.25 (0.30)

[a] State-trait anxiety inventory, Trait version. Scores range from 0 to 60 in the Spanish version of the STAI-T.
[b] $p > .05$. Pearson's χ^2.
[c] $p > .05$. F ratio.

2.2. Stimuli and procedure

We used the paradigm developed by Lissek et al., which consists of three experimental phases (pre-acquisition, acquisition, and generalization) preceded by nine startle habituation trials (cf. Lissek et al., 2008) and which allows the study of both fear conditioning and generalization.

Ten rings of gradually increasing size were presented for 8 s on a computer monitor and served as conditioned stimuli (CSs) and generalization stimuli (GSs). The diameter of the smallest ring was 5.08 cm and subsequent rings increased by 15%. The rings at the two extremes of this size continuum served as CSs. For half of the participants in each anxiety group, the smallest ring was the CS+ (paired with the US before its offset) and the largest was the CS−; for the remaining participants the pairing was reversed. The intermediate rings were used to test conditioned generalization. A fixation-cross appeared on the screen when no stimulus was presented (inter-trial interval, ITI). The US was an electric shock of 100 ms duration, with an intensity adjusted for each participant after a workup procedure as being "highly uncomfortable but not painful", delivered to the volar surface of the right forearm. It was generated by a stimulator (Grass Instruments S48; West Warwick, RI), isolated (SIU5), and transmitted via a constant-current unit (CCU1) to a bipolar bar electrode (EP10-621, Technomed Europe; Beek, NL). Between 3 and 11 shocks ($M = 4.56 \pm 1.73$ SD) were applied in order to arrive at the final intensity. The acoustic startle probe was a 50 ms duration, 102 dB(A) burst of white noise with a near instantaneous rise time, presented binaurally through headphones. Startle probes were presented 4 or 5 s after the beginning of odd trials, inter-probe intervals (IPIs) ranged from 18 to 25 s. ITI durations (9 to 17 s) were adjusted to keep IPIs within the specified range. During even trials, online ratings of perceived risk of shock for each stimulus were obtained (1 = no risk, 2 = moderate risk, 3 = high risk). One or 2 s after trial onset, a question at the top of the screen (Level of risk?) cued participants to respond as quickly as possible using a computer keyboard. Stimulus timing and response recording were controlled by the commercial system Presentation (Neurobehavioral Systems Inc).

Upon arrival at the laboratory, participants read the instructions for the experiment and signed the informed consent. They were not instructed about the CS-US contingency, but were told that they might learn to predict the shock if they attended to the presented stimuli. Next, the electrodes were placed, and the intensity of the shock was adjusted. After placing the headphones, nine startle probes were presented to reduce initial startle reactivity (habituation; results not presented here). Pre-acquisition consisted of six CS+ and six CS− trials presented in the absence of the US; Acquisition consisted of 12 CS+ (nine of them co-terminating with US delivery) and 12 CS− trials. Generalization consisted of 12 CS+ (six of them co-terminating with US delivery), 12 CS−, and six trials from each of the eight GS sizes. Trials for all the phases of the study were presented in quasi-random order with the restriction that no more than two stimuli of the same class appeared consecutively. Furthermore, to ensure an even distribution of trial types, the trials were arranged into two and six blocks for acquisition and generalization phases, respectively. In addition, an equal number of each trial type was used for the recording of psychophysiological measures (recorded in odd trials) and risk ratings (recorded in even trials). ITI trials were intermixed with CS and GS trials across the experimental session (six in pre-acquisition, 12 in acquisition and generalization). In half of the ITI trials, startle probes were also presented. Following Lissek et al. (2008), prior to analyses, responses to every two sizes of GSs were averaged in four classes of responses to GSs (class 1, class 2, class 3, and class 4). There was a 10 min break between the acquisition and generalization. After the experiment, participants rated the discomfort produced both by the US and the startle probe on a 1 (no discomfort) to 10 (maximum discomfort) scale; and answered a multiple-choice question (based on Dawson & Reardon, 1973) regarding contingency awareness ("The electric stimulus usually appeared: (a) in the presence of the smallest ring; (b) in the presence of the biggest ring; (c) randomly; (d) I don't know"). Individuals who correctly identified the stimulus that co-occurred with the US were considered contingency-aware.

2.3. Physiological recordings

Physiological responses were recorded using a Biopac 150 polygraph (Biopac Systems, Inc). The startle blink response was measured by recording the electromyographic activity (EMG) of the orbicularis oculi, using two 0.5 cm Ag/AgCl surface electrodes and following standard guidelines (Blumenthal et al., 2005). Impedance level was maintained below 5 kΩ. The raw EMG signal was sampled at a rate of 2000 Hz, filtered to reduce power line noise (analog 50 Hz notch filter) and to attenuate the frequencies beyond the EMG spectrum (infinite impulse response band-pass filter, cut-off frequencies of 28 and 500 Hz), and then rectified and smoothed off-line