Available online at www.sciencedirect.com
SCIENCE DIRECT®
Behaviour Research and Therapy 43 (2005) 1391–1424
BEHAVIOUR RESEARCH AND THERAPY
www.elsevier.com/locate/brat

Classical fear conditioning in the anxiety disorders: a meta-analysis ☆

Shmuel Lissek[a,*], Alice S. Powers[b], Erin B. McClure[a], Elizabeth A. Phelps[c], Girma Woldehawariat[a], Christian Grillon[a], Daniel S. Pine[a]

[a] *Mood and Anxiety Disorders Program, National Institute of Mental Health, 15K North Drive, Bldg 15k, MSC 2670, Bethesda, MD 20892-2670, USA*
[b] *Department of Psychology, St. John's University, USA*
[c] *Department of Psychology, New York University, USA*

Received 23 October 2003; received in revised form 11 October 2004; accepted 18 October 2004

Abstract

Fear conditioning represents the process by which a neutral stimulus comes to evoke fear following its repeated pairing with an aversive stimulus. Although fear conditioning has long been considered a central pathogenic mechanism in anxiety disorders, studies employing lab-based conditioning paradigms provide inconsistent support for this idea. A quantitative review of 20 such studies, representing fear-learning scores for 453 anxiety patients and 455 healthy controls, was conducted to verify the aggregated result of this literature and to assess the moderating influences of study characteristics. Results point to modest increases in both acquisition of fear learning and conditioned responding during extinction among anxiety patients. Importantly, these patient-control differences are not apparent when looking at discrimination studies alone and primarily emerge from studies employing simple, single-cue paradigms where only danger cues are presented and no inhibition of fear to safety cues is required.
Published by Elsevier Ltd.

Keywords: Classical conditioning; Fear conditioning; Anxiety disorders; Psychophysiology

☆ This work was supported by 'Intramural Research Program of the National Institute of Mental Health'.
* Corresponding author. Tel.: +1 301 402 7219; fax: +1 301 402 6353.
E-mail address: lisseks@intra.nimh.nih.gov (S. Lissek).

0005-7967/$ - see front matter Published by Elsevier Ltd.
doi:10.1016/j.brat.2004.10.007

Introduction

Fear conditioning involves the pairing of a neutral stimulus with an aversive unconditioned stimulus (US). The neutral stimulus initially elicits no emotional reaction, but after repeated pairings with the US, the neutral stimulus becomes a conditioned stimulus (CS) signaling imminent US onset and inducing anxiety associated with the anticipation of the aversive US. Although fear conditioning is generally an adaptive and self-preserving form of learning, such conditioning may become a source of pathology when anxious reactivity to a CS persists in the absence of a CS/US contingency.

Formal theories have implicated fear conditioning in the pathogenesis of anxiety disorders for at least 80 years (Pavlov, 1927; Watson & Rayner, 1920). Renewed enthusiasm for this work (e.g., Gorman, Kent, Sullivan, & Coplan, 2000; Grillon & Morgan, 1999; Pine, 1999) has followed from (1) the introduction of more complex conditioning models accounting for the dynamic context in which fears and anxieties manifest (e.g., Mineka & Zinbarg, 1996), (2) recent findings from basic research in animals delineating specific temporal-lobe circuits engaged by fear conditioning (reviewed by Blair, Schafe, Bauer, Rodrigues, & LeDoux, 2001), and (3) evidence supporting the contributions of similar brain areas to fear learning in humans (e.g., Bechara et al., 1995; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998). Clarification of fear-conditioning differences across anxiety patients and healthy controls is likely to benefit future efforts to elucidate the neurobiological loci of clinical anxiety.

The conditioning model of anxiety disorders, as it was originally formulated, asserted that pathological anxiety (neurosis) develops by way of simple classical conditioning (Pavlov, 1927; Watson & Rayner, 1920). Later theorists expanded on this formulation and shifted toward a model in which classically conditioned fear acts as a drive that motivates and reinforces avoidance (Eysenck, 1976, 1979; Eysenck & Rachman, 1965; Miller, 1948; Mowrer, 1947, 1960). Other permutations of this learning theory emphasized the role of incubation of fear (Eysenck, 1979), evolutionarily prepared aversive associations (e.g., Öhman, 1986; Seligman, 1971), failure to inhibit the fear response to safety cues (Davis, Falls & Gewirtz, 2000), associative learning deficits (Grillon, 2002), stimulus generalization (Mineka & Zinbarg, 1996; Watson & Rayner, 1920), and enhanced *conditionability* (Orr et al., 2000; Peri, Ben Shakhar, Orr, & Shalev, 2000) in the formation and persistence of anxiety disorders.

Although learning accounts of pathological anxiety have been the target of much criticism (for reviews, see Rachman, 1977, 1991), this perspective has received wide support from the psychological and psychiatric communities. Over the years, the model has received validation from three sources: (1) the effectiveness of exposure therapy for treating anxiety disorders (e.g., Barlow, 2002; Marks, 1978), (2) findings pointing to increased rates of pathological anxiety among combat and trauma survivors (e.g., Dohrenwend & Shrout, 1981; Green et al., 1990; Lewis & Engle, 1954), and (3) mixed support from retrospective accounts of conditioning precipitants among anxiety patients (for a review, see Rachman, 1991). A further source of validation may potentially emerge from laboratory-based fear-conditioning studies. From 1947 to date, 20 methodologically heterogeneous studies applying lab-based paradigms to compare fear-conditioning processes between anxiety patients and controls have yielded mixed results. The current study provides a meta-analysis of this literature to (i) clarify the overall effect of fear-conditioning differences among anxiety patients and controls and to (ii) explore the extent to