



Is aversive learning a marker of risk for anxiety disorders in children?

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ABSTRACT

Aversive conditioning and extinction were evaluated in children with anxiety disorders ($n = 23$), at-risk for anxiety disorders ($n = 15$), and controls ($n = 11$). Participants underwent 16 trials of discriminative conditioning of two geometric figures, with (CS+) or without (CS-) an aversive tone (US), followed by 8 extinction trials (4 CS+, 4 CS-), and 8 extinction re-test trials averaging 2 weeks later. Skin conductance responses and verbal ratings of valence and arousal to the CS+/CS- stimuli were measured. Anxiety disordered children showed larger anticipatory and unconditional skin conductance responses across conditioning, and larger orienting and anticipatory skin conductance responses across extinction and extinction re-test, all to the CS+ and CS-, relative to controls. At-risk children showed larger unconditional responses during conditioning, larger orienting responses during the first block of extinction, and larger anticipatory responses during extinction re-test, all to the CS+ and CS-, relative to controls. Also, anxiety disordered children rated the CS+ as more unpleasant than the other groups. Elevated skin conductance responses to signals of threat (CS+) and signals of safety (CS-; CS+ during extinction) are discussed as features of manifestation of and risk for anxiety in children, compared to the specificity of valence judgments to the manifestation of anxiety.

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Introduction

The goal of the current study was to evaluate characteristics of aversive conditioning that may identify the risk for anxiety disorders in children. Childhood and adolescent anxiety disorders are common, with estimates ranging from 5.3% to 17% (see Cartwright-Hatton, McNicol, & Doubleday, 2006, for a review). Also, childhood anxiety poses a risk for adolescent anxiety, which poses an even greater risk for adulthood anxiety and depression (Pine, Cohen, Gurley, Brook, & Ma, 1998). In addition to emotional costs, anxiety disorders in children and adolescents are associated with academic and vocational underachievement (Kessler, Foster, Saunders, & Slang, 1995) and impaired social competence (Spence, Donovan, & Brechman-Toussaint, 1999). Investigation of children at-risk may enhance our understanding of the etiology of this common and costly set of childhood disorders, and inform the development of prevention efforts.

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Risk factors for childhood anxiety disorders include multiple fears and persistent anxiety symptoms (Muris, Merckelbach, Mayer, & Prins, 2000), and temperamental traits of neuroticism and behavioral inhibition (Hayward, Killen, Kraemer, & Taylor, 1998; Schwartz, Snidman, & Kagan, 1999). Parental anxiety is another risk factor, as offspring of parents with anxiety disorders are at 3.5 (range 1.3–13.3) times greater the risk for anxiety disorders than are offspring of control parents (e.g., Merikangas, Avenevoli, Dierker, & Grillon, 1999).

Risk factors themselves do not illuminate mechanisms or pathways by which risk is conferred (e.g., Ormel, Rosmalen, & Farmer, 2004). One such mechanism may be the strength of aversive conditioned responses and their persistence over time. Fear conditioning has long been implicated in the etiology of phobias and anxiety disorders (see Eelen & Vervliet, 2006; Field, 2006). Interest in fear conditioning and extinction has been revived by advances in the basic science of their underlying neurobiology (see Myers & Davis, 2007). Also, etiological models of anxiety disorders recognize the moderating role of individual difference variables (such as ones that place children at-risk for anxiety disorders) upon aversive conditioning (Mineka & Zinbarg, 2006; Ohman & Mineka, 2001).

There is now good evidence for larger conditioned responding during conditioning and more sustained responding during extinction trials in anxiety disordered *adult* samples relative to controls (Lissek et al., 2005). These effects have been measured mostly using skin conductance responses (SCR), an index of changes in general arousal associated with emotional states (Cacioppo, Berntson, Larsen, Poehlmann, & Ito, 2000), and attentional processes associated with the orienting reflex (e.g., Gray & McNaughton, 2000). These effects are most evident in single cue conditioning (i.e., a single conditional stimulus [CS] is paired with an unconditional stimulus [US]) rather than in discrimination conditioning paradigms (i.e., one CS is paired with the US [CS+] and a second is presented alone [CS-]) (Lissek et al., 2005). In discrimination paradigms, anxiety disordered samples typically (but not always) show elevated SCRs to both the CS+ and the CS- during conditioning and extinction compared to controls (e.g., Grillon & Morgan, 1999; Orr et al., 2000; Peri, Ben-Shakhar, Orr, & Shalev, 2000; Veit et al., 2002). Within an associative model, these findings have been interpreted as anxiety disordered individuals displaying elevated fear responding to excitatory cues (CS+ trials) as well as impaired inhibition of fear responding to safety cues (CS- and extinction trials) (Davis, Falls, & Gewirtz, 2000) and overgeneralization from the CS+ to the CS- due to failure to discriminate the stimulus features that distinguish threat from safety cues (see Lissek et al., 2005, for a review). Non-associative explanations of elevated responding to both CS+ and CS- primarily focus on sensitization, or elevated responsiveness to the US and other novel stimuli due to elevated anxious state, and habituation, or decreased responding over repeated presentations of specific stimuli (Lissek et al., 2005).

Only one published study to date has investigated aversive conditioning in anxiety disordered children. Specifically, Liberman, Lipp, Spence, and March (2006) found that both anxiety disordered children and non-anxious controls failed to discriminate between CS+ and CS- trials during acquisition, as indexed by the magnitude of SCRs. However, during extinction, the anxiety disordered group showed larger SCRs (reflecting arousal) as well as larger startle eye blink reflexes (a measure of emotional valence; Lissek et al., 2005) during CS+ than CS- trials. Even though there has been no investigation of these characteristics in children at-risk for anxiety disorders, there is evidence that individual difference variables associated with risk for anxiety disorders moderate aversive conditioning. That is, in unselected samples, more sympathetically aroused individuals show larger SCRs to the CS+ in simple conditioning (Ohman & Bohlin, 1973) and larger SCRs to both the CS+ and CS- during discriminative conditioning and resistance to extinction (Hugdahl, Fredrikson, & Ohman, 1977). Also, traits of anxiety (Spence & Spence, 1966) have been associated with stronger eyelid conditioning, as have traits of anxiety with aversive expectations for avoidance cues (Zinbarg & Mohlman, 1998). Even though the results with trait anxiety are not always consistent (e.g., Guimaraes, Hellewell, Hensman, & Wang, 1991), the combined data pertaining to individual difference variables lends credence to the hypothesis that children at-risk for anxiety disorders may exhibit patterns of conditioning and extinction different from control children.

The goal of this study was to evaluate discrimination conditioning and extinction effects as a potential mechanism by which risk for anxiety disorders is conferred. Rather than selecting children who are at-risk based on their presenting features (such as temperament), we selected children at-risk by virtue of their parental diagnostic status. By so doing, we avoided the tautology of assessing mechanisms of risk in children selected for their manifestation of risk, and capitalized on the reduced heterogeneity inherent to a family study approach (Merikangas et al., 1999). We hypothesized that anxiety disordered children and children at-risk for anxiety disorders would show larger SCRs to the CS+ and the CS- during discrimination conditioning, and larger SCRs to the CS+ during extinction, relative to non-anxious control children. Also, we hypothesized parallel findings in verbal ratings of valence and arousal.

Method

Participants

Participants (Ps) were 49 children (26 boys; 23 girls), aged between 7 years and 12 years, 9 months ($M = 9.42$ years; $SD = 1.62$). At-risk children were recruited from parents attending the UCLA Anxiety Disorders Behavioral Research Program, and from advertisements within the local community and elementary schools in the Los Angeles area (with school district approvals). Anxious and non-anxious control children were recruited through the local community and elementary schools. All children were the biological offspring of their parents.

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