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Fear acquisition and extinction in offspring of mothers with anxiety and depressive disorders

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ABSTRACT

Maternal anxiety and depression are significant risk factors for the development of these disorders in offspring. The pathways through which risk is conferred remain unclear. This study examined fear acquisition and extinction in 26 children at high risk for emotional disorders by virtue of maternal psychopathology ($n = 14$ with a mother with a principal anxiety disorder and $n = 12$ with a mother with a principal unipolar depressive disorder) and 31 low risk controls using a discriminative Pavlovian conditioning procedure. Participants, aged between 7 and 14 years, completed 16 trials of discriminative conditioning of two geometric figures, with (CS+) and without (CS−) an aversive tone (US), followed by 8 extinction trials ($4 \times$ CS+, $4 \times$ CS−). In the context of comparable discriminative conditioning, children of anxious mothers showed larger skin conductance responses during extinction to the CS+ compared to the CS−, and to both CSs from the first to the second block of extinction trials, in comparison with low risk controls. Compared to low risk controls, children of depressed mothers showed smaller skin conductance responses to the CS+ than the CS− during acquisition. These findings suggest distinct psychophysiological premorbid risk markers in offspring of anxious and depressed mothers.

1. Introduction

Anxiety and depression are two of the most common mental health problems affecting children, with 10–20% of school-aged children experiencing emotional disorders during their young lives (Mathews et al., 2011). These disorders cause life-long impairment (Bittner et al., 2007), and are costly to families (Bodden et al., 2008) and national health care systems (Andrews et al., 2004). Parental anxiety and/or depressive disorders are significant risk factors for the development of these disorders in offspring (e.g., Goodman and Gotlib, 1999; Hammen et al., 1990; Rapee et al., 2009; Weissman et al., 1987). Parental depressive disorders are associated with a threefold increase in an individual's risk for developing a depressive episode during adolescence (Hammen, 1997; Williamson et al., 2004). Maternal depression is associated with an earlier onset and more severe course of depression in offspring (Lieb et al., 2002; for a recent review see Gotlib et al., 2006). Similarly, offspring of parents with anxiety disorders are at 3.5 (range 1.3–13.3) times greater risk for anxiety disorders than are offspring of control parents (e.g., Merikangas et al., 1999). Therefore, the investigation of offspring of parents with anxiety and depressive disorders is a powerful strategy to identify premorbid risk markers and early signs of expressions of these conditions.

Learning models emphasise that anxiety develops through the association of a conditioned stimulus (CS+) and an aversive unconditional stimulus (US), and conversely, that anxiety extinguishes through repeated presentation of the CS+ in the absence of the US, which is the underlying

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theoretical framework of exposure therapy (e.g., Bouton et al., 2001; Craske et al., 2009; Davis et al., 2000; Field, 2006; Grillon, 2002; Mineka and Öhman, 2002; Mineka and Zinbarg, 2006; Rachman, 1977; see Vervliet et al., 2012 or Boschen et al., 2009 for reviews). A recent meta-analysis (i.e., Lissek et al., 2005) concluded that within discriminative conditioning studies that require both excitatory responding to a CS+ paired with a US and inhibitory responding to a CS− presented alone, both anxious adults and control adults display comparable levels of differential conditioning, as reflected by larger skin conductance and subjective responses to the CS+ than the CS−. However, anxious adults show overall elevated responses to both CSs compared with control adults, and maintain modestly higher levels of conditioned responding during extinction trials (although this group difference is strongest in CS+ only conditioning procedures) (Lissek et al., 2005).

Basic science research has found similar evidence of larger responding to the CS+ as well as overall elevated responses to both CSs in anxious compared to non-anxious children using discriminative conditioning and extinction experiments (e.g., Craske et al., 2008; Lau et al., 2008; Liberman et al., 2006; Waters et al., 2009). These findings have been interpreted within an associative framework that emphasises elevated fear responding to excitatory cues of threat (i.e., CS+) and impaired response inhibition to signals of safety (CS− and extinction trials) in the pathogenesis of anxiety disorders (e.g., Davis et al., 2000; see Lissek et al., 2005). Another associative account for the findings is overgeneralisation 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 sensitisation, 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).

To date, there is one published study to the authors' knowledge that examines aversive conditioning and extinction in high risk children by virtue of parental anxiety disorders. Craske et al. (2008) found that in the context of similar levels of differential conditioning, as indexed by larger skin conductance responses (SCRs) and subjective evaluations of the CS+ compared to the CS−, high risk children exhibited larger SCRs to the timing of the US on CS+ and CS− trials during acquisition, and larger orienting SCRs to both CSs during extinction trials, in comparison with low risk controls. There were no significant differences in subjective arousal and valence (unpleasantness) ratings between the groups. Overall, findings indicated that children at high risk for anxiety due to parental anxiety displayed larger psychophysiological responses to stimuli signalling threat (CS+) that generalise to cues signalling safety (CS−) and are slower to extinguish in comparison with low risk controls.

Anxiety and depression share numerous risk factors, high rates of comorbidity, and treatment approaches (see Craske and Waters, 2005). However, the specificity of aetiological processes to these disorders is not well understood and an enhanced understanding of common and specific underlying mechanisms would improve knowledge on the pathophysiology of these disorders. To the authors' knowledge, there are no published studies to date that examine differences in aversive conditioning and extinction in offspring of anxious versus depressed and healthy parents. Therefore, the specificity of these learning-based processes as mechanisms by which risk due to parental anxiety versus depression is conferred to offspring remains unclear. However, recent reviews of neurophysiological studies suggest there may be distinct neurophysiological indicators of depression (e.g., Vaidyanathan et al., 2012). For example, findings from startle eye blink modulation experiments suggest that depression is associated with *decreased* fear-potentiated startle, and a flattened affect-startle reflex pattern compared to never-depressed healthy controls (e.g., Allen et al., 1999; Brown et al., 1998; Kaviani et al., 2004; McTeague et al., 2009; see also Vaidyanathan et al., 2012). On the other hand, first and second generation offspring of depressed parents compared to low risk offspring showed *increased* startle reactivity throughout fear-potentiation protocols, similar to that found in anxious adults and offspring of parents with anxiety disorders (e.g., Grillon et al., 2005). In terms of skin conductance measures, evidence suggests that depression, especially endogenous depression, may be associated with lower skin conductance levels and more patients who are SCR non-responders to unpleasant auditory stimuli compared to healthy controls (Lader and Wing, 1964; Mirkin and Coppen, 1980). Varied findings may be due to differing components of depression (e.g., endogenous versus negative affect versus anhedonia), variation in symptom severity, and the methodology and psychophysiological measures employed (see Vaidyanathan et al., 2012 for a review). Nevertheless, these findings primarily point to depression being associated with attenuated psychophysiological responding to negative/stressful stimuli, or the anticipation thereof, and failure to show appropriate reactivity to pleasant stimuli. Together, these findings suggest that depressed individuals may be relatively unaffected by external stimulation (Mirkin and Coppen, 1980), perhaps through the breadth and incessant nature of depressive disorders taking their toll on the human defensive system, thereby reducing psychophysiological reactivity to salient emotional cues (McTeague et al., 2012). Thus, of interest in the present study was whether attenuated psychophysiological responding is a premorbid risk marker that develops during the acquisition of aversive learning in the offspring of depressed parents relative to low risk offspring of never depressed parents.

Based on theoretical accounts of anxiety and depressive disorders (Bouton et al., 2001; Craske et al., 2009; Davis et al., 2000; Field, 2006; Goodman and Gotlib, 1999; Grillon, 2002; Hammen, 1991; Mineka and Öhman, 2002; Mineka and Zinbarg, 2006; Rachman, 1977), the significant comorbidity between them (see Craske and Waters, 2005), and the risk that these disorders pose to offspring of affected parents (see Rapee et al., 2009; Hammen et al., 1990; Weissman et al., 1987), the current study examined aversive Pavlovian conditioning and extinction in the offspring of anxious and depressed mothers compared to mothers without a history of psychopathology. Based on previous