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Offspring of anxious parents: Reactivity, habituation, and anxiety-proneness ☆

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Abstract

Reactivity and habituation patterns were examined in the offspring of anxious and non-anxious parents. Although no differences emerged for magnitude of response to either fear-relevant visual or auditory stimuli, offspring of anxious parents displayed significantly more electrodermal activity during resting baseline and during the inter-trial intervals of these stimulus presentations. Differences also were observed for the number of children per group achieving habituation to the fear-relevant visual and auditory stimuli, where offspring of anxious parents were less likely to habituate to either stimuli. The same pattern of group differences emerged after excluding children diagnosed with an anxiety disorder, indicating that even offspring of anxious parents who did not have an anxiety disorder differ from offspring of normal controls with respect to their pattern of psychophysiological reactivity. It is hypothesized that these features might serve as an indication of anxiety proneness and risk for the development of anxiety disorders.

Keywords: Offspring; Anxious parents; Reactivity; Habituation; Anxiety-proneness

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✠Deceased.
[1]This paper is dedicated to Samuel M. Turner whose untimely death cut short his dedication to understanding the etiology of anxiety in order to improve the life of so many who suffered from these disorders.

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Introduction

Extant data increasingly support the contention that anxiety disorders run in families. Twin studies report higher concordance rates for monozygotic (MZ) than dyzygotic (DZ) twins, with the exception of generalized anxiety disorder (GAD; Andrews, Stewart, Allen, & Henderson, 1990; Torgersen, 1983). Among the specific anxiety disorders, heritability estimates of 30% have been reported for GAD (Kendler, Neale, Kessler, Heath, & Eaves, 1992a) and obsessive-compulsive disorder (OCD; Rasmussen & Eisen, 1992). Furthermore, in one of the largest genetic studies examining evidence for "phobic proneness" (Kendler, Neale, Kessler, Heath, & Eaves, 1992b), heritability was consistent with the familial aggregation of agoraphobia, social phobia, and specific phobia.

Results of family studies supporting a familial factor among adult relatives of adult probands with anxiety disorders date back to the 1980s (e.g., Crowe, 1985; Crowe, Noyes, Pauls, & Slyman, 1983; Harris, Noyes, Crowe, & Chaudry, 1983). More recent studies have focused on the offspring of parents with anxiety disorders and these studies document an increased prevalence of anxiety disorders among children of parents with anxiety disorders when compared to children of normal parents (Sylvester, Hyde, & Reichler, 1988; Turner, Beidel, & Costello,1987; Warner, Mufson, & Weissman, 1995), and in one study, similar findings were reported when the comparison included offspring of dysthymic parents (Turner et al., 1987).

Beidel and Turner (1997) compared rates of psychopathology in the offspring of parents with an anxiety disorder, major depressive disorder, anxiety disorder and major depressive disorder, or no psychiatric disorder. In comparison to the normal control group, rates of psychiatric disorders were significantly greater among the offspring of all three patient groups. Additionally, offspring of anxiety disorders patients were more likely to have only anxiety disorders, whereas those in the other two patient groups were diagnosed with various psychiatric disorders (e.g., depression, externalizing disorders). In another study, the incidence of psychopathology among offspring increased when there was a disorder present, and even more when both parents had a disorder (Merikangas, Avenevoli, Dierker, & Grillon, 1999). Among the offspring, the lifetime prevalence rate for an anxiety disorder was 9.2% when neither parent had an anxiety disorder, compared to 33.7% when one parent had an anxiety disorder and 68.2% when both parents had an anxiety disorder. When specific disorders were examined, similar increasing prevalence rates were found for overanxious disorder (3.9%, 12.5%, and 40.9%); specific phobia (11.5%, 11.5%, and 45.5%); and social phobia (0%, 12.5%, and 36.4%). To summarize, although there are variations based on particular sample characteristics, divergent research approaches reach strikingly similar main conclusions. Offspring of anxious parents are at greater risk for the development of anxiety disorders.

In an effort to identify those most at risk, a number of studies have used psychophysiological reactivity as an index of anxiety proneness. Because the concept of anxiety-proneness may be biologically pre-determined, the assessment of physiological responses to anxiety-evoking event represents an objective method by which to assess this construct. In the majority of these studies, reactivity was assessed when children were exposed to different challenge tasks; typically based on stimuli that were relevant to the parent's fear (e.g., hyperventilation, exposure to spiders; Margraf, Jenkins, & Unnewehr, 1996; Strambi, Brambilla, & Castronovo, 1997). These studies produced mixed results and one possible explanation is that parental fear relevant stimuli may not

necessarily be relevant for the child. In support of this, when variables known to be more generic indicators of fear and anxiety are used (e.g., loud noises), the findings are more clear. Thus, Grillon, Dierker, and Merikangas (1997) examined differences in startle reflex and startle modulation in offspring of parents with anxiety disorders, alcohol disorders, and no psychiatric disorder. When examining startle response to a 106 dB burst of white noise, there was a significantly greater response in offspring of parents with anxiety disorders than offspring of parents with no disorder. Furthermore, over the course of 13 trials, the magnitude of the response was larger in offspring of anxious parents than in offspring of parents in either of the other groups. These offspring were assessed again 6–8 years later when the children averaged approximately 18 years of age. Offspring of anxious parents, in contrast to the other groups, had significantly higher galvanic skin responses during both baseline and threat conditions (i.e., a tone that signaled an aversive event was likely to occur; Merikangas et al.,1999). Although state dependent factors cannot be ruled out, these findings suggest that heightened reactivity as indicated by the galvanic skin response is enduring and might be an indication of anxiety proneness or risk for development of anxiety.

Using heart rate, skin conductance, and muscle tension variables, Turner, Beidel, and Epstein (1991) compared offspring of anxious parents to offspring of parents with no psychiatric disorder. During baseline, offspring of anxious parents had higher resting levels of zygomatic muscle activity and more spontaneous skin conductance fluctuations (SSCF) than offspring of parents with no disorder. During stimuli presentations (a 100 dB tone or a picture of a snake), offspring of anxious parents had significantly more non-event related SSCFs and were significantly less likely to habituate to repeated presentations of these stimuli. Interestingly, despite this very different pattern of autonomic arousal and habituation rate, both groups of children reported only minimal distress during the assessment. Thus, the heightened arousal displayed somatically by the offspring of anxious parents did not appear to be subjectively perceived by the children themselves. One limitation of this study was that a number of the children (primarily those who were offspring of anxious parents) had been diagnosed with anxiety disorders. Thus, it was unclear whether this different pattern of reactivity was simply due to the presence of a pre-existing anxiety disorder or was characteristic of all offspring of anxious parents. Unfortunately, the sample size was too small to examine only the children without a disorder.

Some studies have addressed the issue of pre-existing anxiety disorders in offspring samples via statistical control. For example, when the data in the Grillon et al. (1997) study were re-analyzed controlling for presence of psychiatric diagnoses, increased startle responsivity among the offspring of anxious parents remained significant. Similarly, Grillon, Dierker, and Merikangas (1998) found no significant differences within the high risk group in baseline startle or fear-potentiated startle when the presence of an anxiety disorder was controlled statistically. These findings suggest that even when offspring of parents with anxiety disorders do not have a diagnosable disorder, they still exhibit a pattern of autonomic potential different from the children of normal parents. This specific response profile of reactivity and habituation might serve as an indicator that this group is vulnerable to the development of anxiety disorders. However, this likelihood has not been examined in a study where this potential was subject to methodological control.

To summarize, extant studies indicate that offspring of anxious parents display heightened physiological reactivity to potentially fear producing stimuli. The characteristics are evident

during both tonic and phasic conditions and it has been hypothesized that these features are vulnerability markers for anxiety (Grillon et al., 1997, 1998; Turner et al., 1991). To date, these features have not been examined in a study using methodological control of pre-existing diagnoses in the offspring sample, an alternative to statistically controlling for the existence of current anxiety disorders within the offspring sample. The issue of controlling for the presence of anxiety disorders is important because differential patterns of psychphysiological reactivity between anxiety patients and normal control subjects have long been established (e.g., Lader & Mathews, 1968). Thus, if these physiological responses are to be considered be characteristic of those at risk for the development of anxiety, it is important to demonstrate that the pattern exists in those who are offspring but do not yet have a disorder. Another limitation of extant studies to date is that none have not included a simple control for visual or aural stimulation. Thus, it is unclear if the reported reactivity is a specific response to fearful or startle stimuli or just a response to any type of stimulation. The purpose of this study was to examine reactivity and habituation patterns among offspring of anxious and normal control parents to different stimuli. A second objective was to determine if excluding those children with an anxiety disorder, non-diagnosed offspring of anxious parents have autonomic features different from the offspring of normal control parents. Such a pattern might well be suggestive of anxiety proneness.

Method

Participants

Two groups of parents and their offspring participated in a cross-sectional study of offspring of parents with anxiety disorders. This article describes data related to reactivity and habituation to fear and non-fear relevant stimuli. The anxiety group consisted of families with one parent who had an anxiety disorder (parents and offspring). The control group consisted of parents who were free of psychiatric disorders and their offspring. Each index parent and their spouse was interviewed by a clinician (Ph.D. or doctoral level psychology intern) blind to diagnostic status using the Structured Clinical Interview for DSM-III-R (SCID; Spitzer & Williams, 1986). To determine inter-rater reliability, 22% of the SCID interviews were randomly selected to be videotaped and scored by a second clinician unaware of the parent's diagnosis. The reliability coefficient was $\kappa = .95$ for the presence of the primary SCID diagnosis.

Among parents with an anxiety disorder, 49% ($n = 16$) were diagnosed with panic disorder with or without agoraphobia, 27% ($n = 9$) with generalized anxiety disorder, 15% ($n = 5$), with obsessive-compulsive disorder, 6% ($n = 2$) with social phobia, and 3% ($n = 1$) with subthreshold agoraphobia without panic disorder. All anxiety disorders were primary. Approximately 71% ($n = 24$) of the anxious parents were diagnosed with a comorbid Axis I disorder consisting of an additional anxiety disorder or dysthymia. All diagnoses were current. The index parent's spouse did not suffer from any current or life-time psychiatric disorder. Among the control group participants, neither the index parent nor their spouse met criteria for any current or lifetime anxiety disorder. However, one mother had a history of panic attacks in college, prior to the birth of her child, but not since that time. Approximately 24% of anxious parents and 54% of non-anxious parents were recruited from the Pittsburgh area with the remainder recruited in

Charleston, SC. Anxious patients were recruited through established Anxiety Disorders clinics in both areas and normal control families were recruited through newspaper advertisements seeking participation of families and children to participate in a study of "fear development". There were no differences in demographic variables across sites with the exception of a larger number of African American participants at the Charleston site. Group demographic information is presented in Table 1.

There were 47 offspring of anxious parents and 43 offspring of normal control parents in the sample. Of the 64 families, 26 families (13 of 34 families with an anxious parent and 13 of 30 families with a normal control parent) had more than one child who participated in the study. In total, 72% of the anxious parent group had one sibling participant vs. 70% of the control group. Approximately 23% of the anxious parent group had two sibling participants as did 28% of the control group. Finally, approximately 4% of anxious parents and 2% of control parents had three child participants. No differences in the number of offspring (1, 2, or 3) by parent group were observed (χ^2 (2) = .45, $p > .05$). No monozygotic or dizygotic twins participated in the study.

All children were between the ages of 7 and 12 years, resided with at least one biological parent (i.e., the index parent), and were of normal intelligence as measured by the WISC-III Vocabulary and Block Design subscales. No family member had a major chronic physical illness (e.g., cancer, diabetes, etc.). Diagnostic interviews were conducted using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Chambers, Puig-Antich, & Hirsch, 1985)

Table 1
Group demographic information

	Offspring of non-anxious parents	Offspring of anxious parents
Index parent		
Gender (% female)	93.3	85.3
Race (%)		
Caucasian	93.3	85.3
African American	6.7	14.7
Marital status (%)		
Married	66.7	70.6
Divorced/separated	23.3	14.7
Remarried	6.7	5.9
Other/single	3.3	8.8
Age (years; *M* (SD))	37.0 (4.98)	36.9 (4.90)
SES (Hollingshead scale; *M* (SD))	40.9 (12.77)	34.7 (15.48)
Children		
Sex (% female)	47.6	40.0
Race (%)		
Caucasian	95.2	86.7
African American	4.8	13.3
Age (years; *M* (SD))	10.2 (1.7)	10.1 (1.8)

Note: $n = 34$ for anxious parents; $n = 30$ for non-anxious parents; $n = 47$ for children of anxious parents; $n = 43$ for children of non-anxious parents.

Table 2
Frequency of childhood anxiety disorders by parent group

	Offspring of non-anxious parents	Offspring of anxious parents
Anxiety disorder		
Overanxious disorder	—	4
Specific phobia	1	2
Avoidant disorder	—	1
Obsessive–compulsive disorder	—	1
Social phobia	1	1
Separation anxiety disorder	—	1

Note: Four children of anxious parents qualified for a comorbid anxiety disorder including two cases of separation anxiety disorder, one case of anxiety disorder/NOS, and one case of specific phobia.

as modified by Last (1986). Parents were interviewed first, followed by the child alone, by a clinician blind to parental diagnosis. Diagnoses were assigned based on combined report of the parent and child. All diagnoses were current. To determine inter-rater reliability, 29% of the K-SADS interviews were randomly selected to be videotaped and scored by a second clinician unaware of the parent or child's diagnosis. The reliability coefficient was $\kappa = .68$ for the K-SADS (in two K-SADS cases, clinicians disagreed on severity but not presence/absence of the disorder. These two cases were coded as disagreements.). Significantly more children of anxious parents ($n = 17$; including two cases of specific phobia) met criteria for an Axis I diagnosis compared to offspring of control parents ($n = 3$; including one case of specific phobia; χ^2 (1) = 11.47, $p < .001$; see Table 2 for specific diagnoses).

Further examination of child diagnoses indicated that 24% ($n = 11$) of children of anxious parents were diagnosed with an anxiety disorder compared to 4.7% ($n = 2$) of children of control parents (χ^2 (1) = 6.61, $p = .01$). Table 2 lists the primary anxiety disorder diagnoses. In addition to the primary diagnosis, 6.4% ($n = 4$) of children of anxious parents had a second (comorbid) anxiety disorder vs. 0% of offspring of control parents but this difference did not reach statistical significance (χ^2 (1) = 2.84, $p > .05$). Finally, several children in each group had disorders other than anxiety. Among children of anxious parents, there were two cases of Major Depressive Disorder, two cases of Dysthymia, one case of Adjustment Disorder with Depressed Mood, and two cases of Attention-Deficit/Hyperactivity Disorder. Among children of control parents, one child received a diagnosis of Oppositional Defiant Disorder.

Assessment procedure

Three assessment stimuli were used: an 8 s, color picture of a snake (visual stimulus), a 1 s, 1000 Hz, 100 db tone (auditory stimulus), and an 8 s, color picture of a daffodil (neutral stimulus). The neutral stimulus was included to control for the presence of a visual cue. Order of stimulus presentation was randomly determined. Each stimulus was presented for 20 consecutive trials, with an inter-trial interval of 30 s. Stimuli and ratings of subjective distress were pre-recorded on videotape to insure accurate timing of presentation and were presented on a 21-in color television monitor. Finally, a marker was automatically placed in participants' physiological data file to indicate onset and offset of all stimuli.

Measures of reactivity

Both skin conductance and heart rate responses to the presentation of the stimuli were measured. Reactivity was assessed by computing difference scores (peak stimulus level minus pre-stimulus level = difference score) for both heart rate and skin conductance. An additional measure of reactivity was the frequency of SSCFs that occurred during baseline as well as the inter-trial intervals during each series of 20 stimulus presentations and during the inter-trial interval (i.e., occurred in the absence of a stimulus). An SSCF was operationalized as an increase of 0.05 microsiemens (μS) that occurred during the inter-trial interval (i.e., in the absence of a stimulus).

Measures of habituation

Habituation was operationally defined as no SCR or a SCR less than .05 microsiemens (μS) for three consecutive stimulus presentations. Both the percentage of each group who achieved this habituation criterion as well as the number of trials until habituation was achieved were used as indices of habituation. When calculating rates of habituation, children who never responded to the stimuli presentation were excluded from the analyses. Non-responders were defined as those children who did not exhibit a SCR equal to or greater than .05 μS to one of the first five stimulus presentations.

Measure of subjective distress

Following the 20th presentation of each stimulus, children completed a five point visual rating scale that was adapted from the Self-Assessment Manikin (SAM; Lang & Cuthbert, 1984). Each child rated their level of fear using a series of five pictures portraying varying degrees of emotional distress. This five point scale has been used in many previous studies of childhood anxiety and appears to be a valid measure of self-reported fear (e.g., Turner et al., 1987).

Procedure

To ensure electrode surface de-polarization, all electrodes were soaked in a saline solution for several hours before application. Skin conductance (SC) was recorded from the participant's non-dominant hand in the manner recommended by Fowles et al. (1981) using two Beckman silver/silver chloride 1 cm^2 electrodes filled with Hewlett-Packard Redux skin conductance paste. Before attaching SC electrodes, participants' thenar eminence and hypothenar eminence (i.e., inside palm) were gently swabbed with commercially available isopropyl rubbing alcohol (70% by volume) to remove excess oil and pre-existing sweat. SC electrodes were then attached to the inside palm using disks of double sided adhesive tape (3 M, MN, USA). A Coulbourn S71-23 isolated skin conductance module measured skin conductance by means of a constant voltage circuit. EKG (i.e., heart rate) electrodes were placed on the child's chest (i.e., sternally on the xiphoid process and below the left floating rib). Cardiac changes were measured by a Coulbourn S75-05 Hi Gain Bioamplifier and Bandpass Biofilter S75-38 inputting to a Coulbourn S77-26

Tachometer. The low filter was set at 1 Hz and the high filter was set at 150 Hz. For female participants, only a female experimenter was allowed to attach electrodes.

The assessment was conducted in a dimly lit, temperature and humidity controlled, sound-attenuated room. Experimenter and equipment were located in an adjacent room but the child remained in constant contact via a one-way mirror or video camera and a two-way intercom. After attaching electrodes, each child was instructed on how to make subjective ratings using the SAM. To minimize movement artifacts, the child sat in a large, comfortable recliner and was instructed to sit as quietly as possible. If the child moved, a "noise" button was activated and placed a marker in the child's data file, preventing scoring of movement artifacts. Children sat quietly for 20 min (10 min acclimation period followed by a 10 min baseline period). During this time, tonic (resting) levels of heart rate and skin conductance were monitored. Following the baseline, the psychophysiological stimuli were presented as described above.

Data reduction and analytic plan

Baseline values for heart rate and skin conductance level were computed using only the last "clean" (i.e., no movement) minute of the 10 min baseline period. Difference scores for trials 1, 5, 10, 15, and 19 served as a repeated measures factor in subsequent analyses. Because participants made SAM ratings immediately following presentation of stimulus #20 (possibly confounding response values), scores for stimulus #19 were used in all repeated measures analyses. As a general note, the *n* varies slightly across analyses due to missing data points, primarily resulting from movement artifacts.

Because the sample contained some families with multiple offspring, all observations cannot be considered independent, an assumption required for the general linear model (GLM). Thus, the SAS mixed model procedure that allows for modeling of variance associated with the inclusion of multiple offspring by treating the family as a nested cluster (i.e., child within parent) was used. The explanatory/independent variables included both fixed effects (e.g., parent diagnostic group, stimuli) and random effects (i.e., family and child participants). The autoregressive (i.e., type = ar(1)) covariance structure, which specifies the covariance structure for the residuals, was used for all repeated measures analyses. This covariance type applies to repeated measures designs in which observations in close proximity to one another are more highly correlated than those not in close proximity (e.g., trial 1 is more highly correlated with trial 5 than trial 19). For analyses with no repeated measurements, the compound symmetry covariance type was selected. Denominator degrees of freedom were estimated using the Satterthwaite approximation (DDFM = Satterth) which adjusts degrees of freedom for the approximate *F*-statistics.

Dependent variables included baseline physiological levels of heart rate, skin conductance, and SSCFs as well as heart rate reactivity and skin conductance reactivity and habituation. SSCFs during the stimulus inter-trial intervals also was assessed. Both heart rate and skin conductance variables were assessed. Each reactivity variable was examined independently with the model statement including group (anxious parent vs. non-anxious parent group), stimulus type (tone, snake, daffodil), and the repeated measurement trials for the physiological variables (i.e., Group × Stimulus × Type × Trial). The full factorial model (i.e., all main and inter-active effects) was examined. Number of SSCFs and habituation variables were examined separately for each stimulus using GEE analysis (Liang & Zeger, 1986) that allows analysis of correlated data

(i.e., measurements from multiple siblings). A Bonferroni corrected alpha was used in all post hoc analyses.

Results

Baseline

No significant differences were detected for baseline heart rate or skin conductance level [p's $> .05$]. However, significant group differences were observed for the frequency of SSCFs [F (1, 53.6) $= 6.46$, $p < .02$], with children of anxious parents exhibiting a two-fold increase in fluctuations compared to children of non-anxious control parents ($M = 28.82$ vs. $M = 13.47$). Group means and standard deviations for each variable are presented in Table 3.

Cardiac reactivity

Heart rate difference scores revealed significant Stimulus Type and Trial main effects [F (2, 324) $= 24.07$, $p < .001$; F (4, 708) $= 2.40$, $p < .05$]. With respect to Stimulus, the difference score was significantly smaller for the tone ($M = 7.5$, $SE = .66$) when compared to the snake ($M = 11.82$, $SE = .67$; t (323) $= -6.73$, $p < .01$) and flower ($M = 10.59$, $SE = .68$; t (321) $= -4.75$, $p < .01$). With regards to Trials, no between-trial differences reached significance when the Bonferroni correction was used. Furthermore, although a significant Group $\times$ Trial interaction emerged (F (4, 708) $= 3.56$, $p < .01$), examination of simple effects using the Bonferroni correction revealed no significant group differences. No other main effects or interactions were observed.

Skin conductance reactivity

There were significant Stimuli and Trial main effects [F (2, 212) $= 24.45$, $p < .001$; F (4, 626) $= 27.21$, $p < .001$, respectively]. For the Stimuli main effect, mean SCR values for the tone stimulus ($M = .30\,\mu S$) was larger than for the snake ($M = .15\,\mu S$; t (211) $= 5.72$, $p < .001$) or daffodil ($M = .14\,\mu S$; t (212) $= 6.28$, $p < .001$), with no significant mean difference emerging between the latter two stimuli [t (215) $= .66$, $p > .05$]. For the trial effect, SCR magnitude for

Table 3
Group means and standard deviations for baseline physiological measures

	Offspring of non-anxious parents	Offspring of anxious parents
Skin conductance level	5.0 (1.9)	5.2 (2.2)
Heart rate	81.6 (9.5)	82.4 (10.2)
# of spontaneous fluctuations	13.2 (14.3)	28.4 (30.4)**

Note: **$p < .001$; Heart rate is reported in beats per minute; Skin conductance level is reported in μS.

trial 1 was significantly larger compared to trials 5, 10, 15 and 19, with SCR values generally decreasing across trials [$t_{\text{trial 1 v. 5}}$ (609) = 8.39, $t_{\text{trial 1 v. 10}}$ (882) = 8.03, $t_{\text{trial 1 v. 15}}$ (902) = 8.93, $t_{\text{trial 1 v. 19}}$ (807) = 7.93, all p's < .001]. Thus, reactivity to the first stimulus presentation was larger than that for the subsequent presentations. Finally, a significant Stimuli × Trial interaction was observed [F (8, 915) = 6.30, $p < .001$]. As illustrated in Fig. 1, SCR values during trials 1 and 5 of the tone stimulus were significantly larger than SCR trial values for the snake [$t_{\text{trial 1}}$ (663) = 6.65, $t_{\text{trial 5}}$ (675) = 8.39, p's < .001] or flower [$t_{\text{trial 1}}$ (731) = 6.06, $t_{\text{trial 5}}$ (710) = 6.47, p's < .001]. All other interactions (i.e., Group × Stimulus Type, Group × Trial, Group × Stimulus Type × Trial) were non-significant [$p > .05$]. Thus, it is clear that the fearful stimuli elicited the expected responses but there were no group differences.

During the tone ITIs [F (1, 37.8) = 5.69, $p < .05$], offspring of anxious parents ($M = 26.28$) exhibited significantly more SSCFs compared to children of non-anxious parents ($M = 16.89$). For the snake condition [F (1, 50.9) = 7.69, $p < .01$], offspring of anxious parents again exhibited significantly more spontaneous fluctuations than children of control parents ($M = 21.85$ vs, $M = 11.35$, respectively). No differences in SSCFs were found for the daffodil stimulus [F (1, 55.7) = .84, $p > .05$], suggesting that responses are not a product of simple visual stimulation.

Habituation

To examine differential rates of habituation, the groups were compared on two indices: (1) number of children per group who habituated and (2) number of trials to achieve habituation. Children who did not exhibit an initial response to one of the first five stimulus presentations were categorized as non-responders and excluded from this analysis, resulting in 38 children of non-anxious parents and 43 children of anxious parents for the tone stimulus. For the snake stimulus, 33 children of non-anxious parents and 37 children of anxious parents were included. Finally, for the flower stimulus, 31 children of non-anxious parents and 37 children of anxious parents were

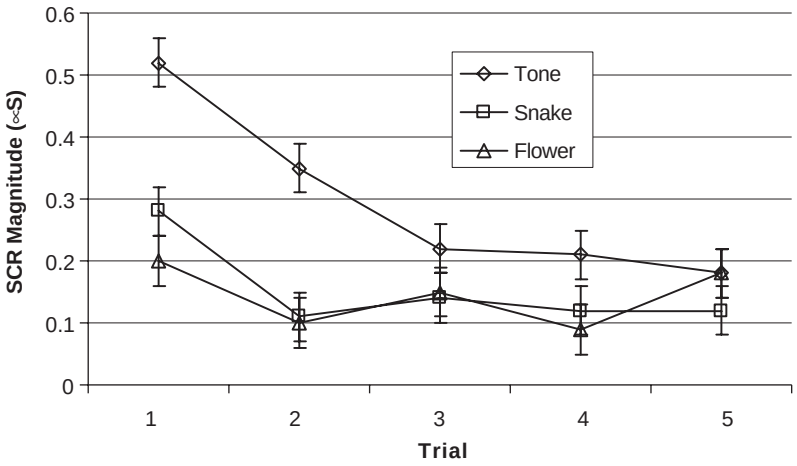

Fig. 1. Mean SCR values for the stimulus type × trial interaction.

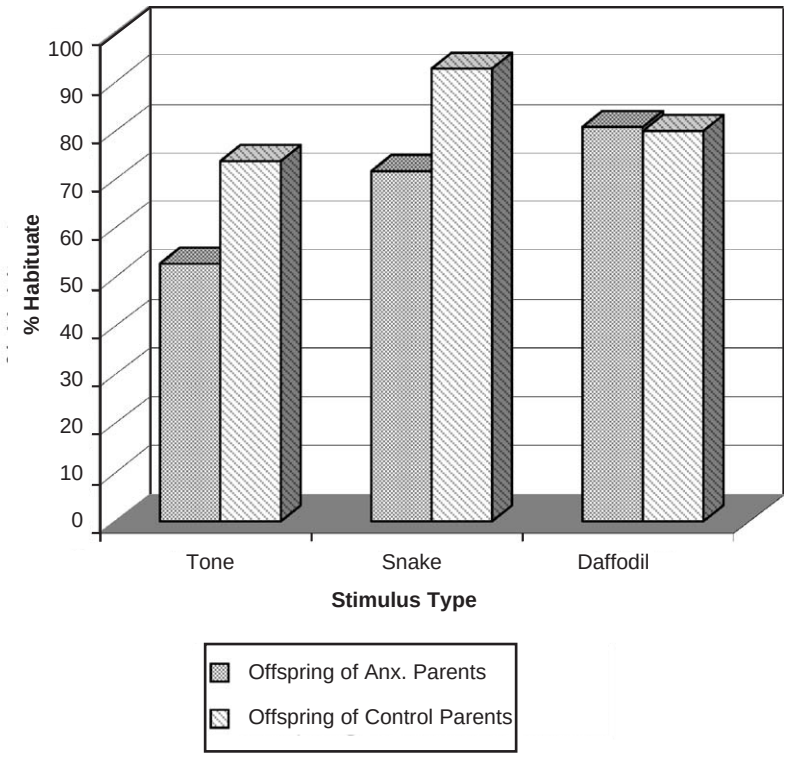

Fig. 2. Percentage of children of anxious vs. non-anxious parents reaching habituation per stimulus type.

included in the analysis. Significant differences emerged for the tone stimulus (χ^2 (1) = 3.83, $p < .05$). The computed odds ratio indicated that children of anxious parents were approximately 3 times less likely to habituate to the tone compared to offspring of non-anxious parents. There was also a group difference with respect to habituation to the snake stimulus (χ^2 (1) = 5.02, $p < .05$) with offspring of anxious parents being over 5 times less likely to habituate. As expected, habituation rates did not differ for the flower stimulus (χ^2 (1) = .54 $p > .05$). Results for the three stimuli are depicted in Fig. 2.

The second habituation variable, number of trials to reach habituation, indicated that the groups differed significantly for the tone stimulus [F (1, 75) = 3.85, $p = .05$]. Children of anxious parents required more trials to achieve habituation ($M = 14.6$) than did children of non-anxious parents ($M = 11.8$). Although the difference did not reach statistical significance, perhaps due to lowered power resulting from the elimination of 10 offspring and normal controls and 10 offspring of anxious parents [F (1, 13) = 3.69, $p = .06$], the offspring of anxious parents required more trials ($M = 9.5$) to achieve habituation than the offspring of non-anxious control parents ($M = 6.0$) during the snake condition. No significant Group differences emerged for number of trials to reach habituation for the flower stimulus [F (1, 41.2) = .16, $p > .05$], indicating that the response difference only emerges when potentially fear producing stimuli are present.

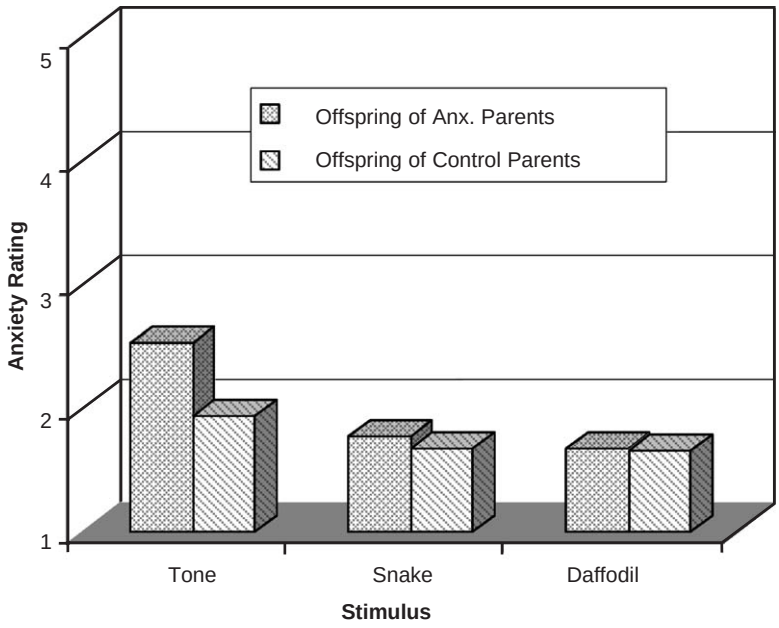

Fig. 3. Distress ratings for offspring of anxious and normal control parents.

Anxiety self-ratings

There was a main effect for Stimulus [$F(2, 193) = 13.13$, $p < .001$]. Anxiety ratings were highest for the tone stimulus ($M = 2.23$) compared to the snake ($M = 1.73$; $t(193) = 4.16$, $p < .001$) or flower ($M = 1.66$; $t(193) = 4.66$, $p < .001$). As illustrated in Fig. 3, there was a significant Group × Stimulus Type interaction [$F(2, 193) = 3.48$ $p < .05$], with offspring of anxious parents ($M = 2.5$) endorsing greater anxiety during the tone stimulus compared to children of non-anxious parents ($M = 1.9$, $t(128) = -2.59$, $p < .02$).

Re-analyses excluding children with a diagnosis

When the data were reexamined excluding all children diagnosed with an anxiety disorder, the pattern of results did not change. Specifically, for heart rate reactivity, there were main effects for Stimulus ($F(2, 267) = 17.28$, $p < .001$) and Trials ($F(4, 593) = 3.26$, $p < .05$) as well as a significant Trial × Group interaction. Heart rate increase for the tone condition ($M = 7.7$) was significantly smaller than the snake condition ($M = 11.63$, $t(269) = 5.7$, $p < .001$) and the flower condition ($M = 11.0$, $t(263) = 4.2$, $p < .001$) whereas the latter two were not significantly different. For trials, the mean response for trial 1 ($M = 8.8$) was significantly higher than for trials 15 ($M = 11.2$; $t_{\text{trial 1 v. 15}}(704) = 2.87$) and 19 ($M = 11.0$, $t_{\text{trial 1 v. 19}}(698) = 2.60$) both p's $< .05$. Similarly reactivity for trial 10 ($M = 9.03$) was significantly higher than for trial 15 ($t_{\text{trial 10 v. 15}}(502) = 2.52$) and trial 19 ($t_{\text{trial 10 v. 19}}(708) = 2.20$). The overall ANOVA indicated a significant Trial × Group interaction ($F(4, 708) = 3.56$, $p < .01$) although none of the individual comparisons achieved the conventional level of statistical significance.

For skin conductance, there were main effects for Stimulus (F (2,180) = 20.18, $p<.001$) and Trials (F (4, 523) = 19.48, $p<.001$) and a significant Trial by Stimulus interaction (F (8, 521) = 4.44, $p<.001$). Trial 1 was significantly higher than for all other trials ($t_{\text{trial1 v. 5}}$ (504) = 7.12, $t_{\text{trial1 v. 10}}$ (743) = 6.75, $t_{\text{trial1 v. 15}}$ (750) = 7.56,$t_{\text{trial1 v. 19}}$ (674) = 6.56, all p's$<.001$). For the Stimulus main effect, response to the tone ($M = .30$) was significantly higher than for the snake ($M = .15$, t (180) = 5.26, $p<.001$) or the flower ($M = .14$, t (180) = 5.66, $p<.001$) with no significant difference for the latter two conditions, t (181) = .49, $p>.05$). Finally, for the significant Trial × Stimulus interaction, SCR values during Trials 1 and 5 of the tone condition were significantly larger than for the snake ($t_{\text{trial 1}}$ (580) = 5.45, $t_{\text{trial 5}}$ (636) = 5.30, p's$<.001$) or the flower stimulus ($t_{\text{trial 1}}$ (586) = 7.21, $t_{\text{trial 5}}$ (610) = 5.51, p's$<.001$).

Children of anxious parents had a significantly higher frequency of baseline SSCFs ($M = 33.4$) than the children of normal control parents ($M = 13.4$; F (1,51) = 10.18, $p<.01$). They also had higher frequencies of SSCFs during both the tone ($M = 29.5$ vs. $M = 17.5$; F (1,45) = 6.07, $p<.05$) and the snake conditions ($M = 25.8$ vs. $M = 11.1$; F (1,44) = 12.06, $p<.01$).

For habituation, there were significant group differences for the tone (χ^2 (1) = 4.10, $p<.05$) and snake (χ^2 (1) = 4.92, $p<.05$) conditions. Compared to offspring of normal control parents, children of anxious parents were approximately 4 times less likely to habituate to the tone condition and over 5 times less likely to habituate to the snake condition. Again, as expected, there were no group differences for the flower condition (χ^2 (1) = 0.27, $p>.05$).

Additionally, there were significant group differences on the number of trials to achieve habituation for the tone [$M = 15.2$ (offspring of anxious children) vs. $M = 11.9$ (offspring of normal control parents); F (1,45) = 4.13, $p<.05$] and snake condition [$M = 11.2$ (offspring of anxious parents) vs. $M = 6.0$ (offspring of normal control parents); F (1,40) = 6.53, $p<.05$] but not for the flower condition [$M = 8.8$ (offspring of anxious parents) vs. $M = 9.4$ (offspring of normal control parents); F (1,34) = .07, $p>.05$].

Finally, there was a significant main effect for stimulus for the subjective ratings of distress (F (2, 146) = 10.00, $p<.001$). Distress ratings ($M = 2.32$) were higher for the tone than for the snake condition ($M = 1.82$; t (145) = 3.57, $p<.001$) or the flower condition ($M = 1.75$; t (146) = 4.10, $p<.001$). However, in the reduced sample, the Group × Stimulus interaction did not reach statistical significance, and mean scores were in the mild range ($M = 2.11$ for the offspring of anxious parents vs. $M = 1.81$ for the children of non-anxious parents).

Discussion

Consistent with prior research (Grillon et al., 1997, 1998; Merikangas et al., 1999; Turner et al., 1991), results of this study indicate that the offspring of anxious parents exhibit a pattern of psychophysiological reactivity that is different from that of offspring of parents without a psychiatric disorder. These differences are evident during both resting and challenge conditions. During baseline, offspring of anxious parents exhibited twice as many SSCFs as the offspring of normal control parents. Grillon et al. (1997) did not assess differences in resting baseline, but they did find differences in the magnitude of baseline startle (eye blink reflex in the absence of a warning stimulus) and concluded that this group difference could be (a) trait-related, reflecting a tonic characteristic independent of an emotional state or (b) a phasic, state-related change

reflecting anticipation of the upcoming task. Although the results of these studies are not directly comparable (baseline startle magnitude in the Grillon et al. (1997) study was in response to a stimulus event, whereas spontaneous fluctuations in this study were in the absence of an event), the two hypotheses put forth to explain those results are relevant to the findings presented here. That is, both outcomes suggest that offspring of anxious parents appear more physiologically aroused than the offspring of normal parents. This suggests that these offspring are more likely to have psychophysiological characteristics that are different from the offspring of normal parents, and that these differences might be indicative of a heightened proclivity to react to fearful stimuli and thus could be a risk factor for the development of anxiety disorders. However, it should be noted that these experimental paradigms are novel situations (e.g., children have electrodes attached and may be in sound-attenuated chambers). It is possible that the children are reacting to the novelty of the experimental situation and that the findings do not represent their typical arousal state. Thus, these responses still could be state-determined rather than trait-related and therefore, the state-vs.-trait distinction remains unclear.

Unlike Grillon et al. (1997, 1998), this study did not find group differences in response magnitude when children were presented with either an auditory (tone) or visual (snake) stimulus. Merikangas et al. (1999) reported significantly greater galvanic skin response (GSR) among offspring of parents with anxiety disorders when compared to offspring of parents with substance abuse disorders or offspring of normal controls. In that study, the offspring of anxious parents had higher baseline GSR, which became even more pronounced in the threat condition. There are numerous differences in the methodology of the studies that might account for these disparate findings, including the specific response variable under study (eye blink vs. skin conductance), the particular stimuli (white noise vs. tone or visual presentations), and the particular paradigm (conditioning vs. habituation). A careful series of studies addressing each of these factors will be necessary to further isolate the critical factor.

Although this study, as well as others (Margraf et al., 1996), did not reveal group differences in responses to stimuli presentation, the offspring of anxious parents in this study had significantly more spontaneous fluctuations (inter-stimulus interval arousal) during the fear relevant conditions. As noted in Turner et al. (1991), these findings suggest a defect in the ability of these children to adapt easily to novel or stressful stimuli, a hypothesis further supported by their differential habituation patterns. If further confirmed, it would suggest that there is a basic defect in adaptability in offspring of anxious parents. Thus, even if as suggested above, this pattern of reactivity is specific to novel situations and events, it would still suggest a basic deficit in adaptability. It would remain to be determined if this defect is biological in origin, psychological in origin, or some combination. Also, consistent with the earlier study, the groups differed in rates of habituation to the snake and the group difference approached significance for the tone condition. Using a different measure of habituation (i.e., number of trials to habituation), the offspring of control parents habituated more rapidly than the offspring of anxious parents. Therefore, using two different measures and two different types of stimuli, these data provide further support for the hypothesis of a fundamental difference in the skin conductance characteristics of offspring of anxious parents. This could explain why some events seem to have an adverse effect on some children but not others. In other words, some are more prone to be anxious than others, and once the fear is activated, habituation does not take place.

It is important to note that the offspring of anxious parents did not show a significantly different frequency of spontaneous fluctuations and habituation rates in response to all events but rather only to fear relevant stimuli. The tone and the snake were selected because of their theoretical relevance to fear conditioning. Loud noises, for example, often are used as a UCS (as in Grillon et al., 1997, 1998) and snakes are commonly feared objects (Agras, Sylvester, & Oliveau, 1969). Differential physiological responses of the two groups during the tone and snake conditions, but not during the flower condition, suggests some degree of specificity. That is, the offspring "at risk" for the development of anxiety disorders may not be detectable by their typical daily behaviors, but only when placed in situations that have the potential to be arousing or fear-producing. Other research (cf., Kagan, Reznick, Clarke, Snidman, & Garcia-Coll, 1984; Suomi, 1986) using behaviorally inhibited children or rhesus monkeys bred for high anxiety show similar patterns of responses when under fear-relevant conditions.

An interesting finding is that the differences in psychophysiological responsiveness were sometimes outside the child's awareness. Although higher distress ratings during the tone were evident for offspring of anxious parents, both groups of children reported low and non-significantly different levels of distress, despite differences in reactivity during baseline as well as in the snake presentation. This low level of emotional arousal also was reported by Turner et al. (1991) and suggests that children of anxious parents sometimes do not perceive themselves to be aroused, even when their physiological reactivity indicates otherwise. This also suggests that children with these characteristics likely will go unidentified when participating in normal everyday activities. Whether these features prove to be predictive of psychopathology, however, remain to be determined.

The findings reported above, like those of other studies, may be criticized because children who already had an anxiety disorder were included in the offspring samples, and these children are more likely to be represented among the offspring of anxious parents than among the offspring of normal control parents. Thus, we repeated the analysis using only offspring of anxious parents without an anxiety disorder and the group differences were replicated. These findings suggest that the physiological reactivity noted in the offspring of anxious parents is not a function of pre-existing anxiety conditions. Rather, this reactivity exists even among children who do not meet criteria for any disorder. At a minimum, this finding suggests that as a group, the offspring of anxious parents, not just those who have a diagnosed disorder, have psychophysiological features different from those of offspring of normal parents and those with other psychiatric disorders. However, at least two questions regarding these differences still need to be answered: do these differences indicate a basic difference (perhaps biological) and are they predictive of anxiety disorder development?

Finally, in this study, skin conductance (magnitude of response, spontaneous fluctuations, and rate of habituation) appears to be a more sensitive measure of reactivity than heart rate. These findings are consistent with those of Turner et al. (1991) and Grillon et al. (1998). As noted (Turner et al., 1991), the length of the stimuli presentations may have been too short in duration for accurate detection of heart rate changes. Longer tasks, such as reading aloud in front of a group, may be necessary to detect changes in heart rate reactivity.

These data are potentially important because if confirmed, they might contribute to a better way to predict those who are at high risk for anxiety disorders (other than just familial status or anxiety sensitivity). For example, because not all members of a family develop disorders, the

addition of an objective measure, such as psychophysiological response, may help to further clarify those as risk. Furthermore, unlike anxiety sensitivity measures that depend upon self-report, and are therefore subject to response bias (e.g., boys tend to underreport their anxiety on self-report measures), psychohysiological assessment data are objective and are much less likely to be manipulated by the subject. Also, if these findings are confirmed, they might shed some light on the issue of familial anxiety. For example, they might be used to explain why although anxiety disorders are familial, frequently the disorders are not the same. That is, the familial feature might be the heightened arousal indicated by these variables rather than a specific disorder. Thus, heightened physiological response might be a necessary but not sufficient factor for the development of anxiety disorders. Those at high risk might then develop a specific disorder depending on their individual experiences, again reinforcing the roles of both biological vulnerability and environmental factors in the etiology of anxiety disorders.

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