

Pupillary reactivity to emotional stimuli in children of depressed and anxious mothers

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Background: The primary aim of this study was to examine differences in physiological reactivity (measured via pupillometry) to emotional stimuli between children of depressed versus nondepressed mothers. A second goal was to examine differences in pupil dilation to emotional stimuli between children of anxious versus nonanxious mothers.

Method: Participants included 117 mother-child pairs drawn from the community. Children were between the ages of 8 and 14. Pupil dilation was assessed using an eye-tracker while participants viewed angry, happy, or sad faces.

Results: Children of mothers with a history of major depression (MDD) exhibited increased pupil dilation to sad, but not happy or angry, faces compared with children of nondepressed mothers. Second, we found that children of anxious mothers exhibited increased pupil dilation to angry, but not happy or sad, faces compared to youth of nonanxious mothers. **Conclusions:** The current findings add to the growing body of research suggesting that differences in physiological reactivity to depression- and anxiety-relevant cues may represent an important mechanism in the intergenerational transmission of MDD and anxiety. **Keywords:** Pupil dilation, vulnerability, depression, anxiety, intergenerational transmission.

Cognitive models of depression and anxiety emphasize the role of biased processing of disorder-specific stimuli (e.g., Clark, Beck, & Alford, 1999). Consistent with these models, research has shown that depressed adults exhibit attentional biases specifically to depression-relevant stimuli (e.g., sad faces), whereas individuals with anxiety disorders exhibit attentional biases specifically to threat-relevant stimuli (e.g., angry or fearful faces; for reviews, see Peckham, McHugh, & Otto, 2010). Although the majority of this research has been conducted with adults, there is growing evidence for similar patterns of specificity in youth. For example, one study found that whereas currently depressed youth exhibit attentional biases specifically for sad faces, youth with a current anxiety disorder exhibit attentional biases specifically for angry faces (Hankin, Gibb, Abela, & Flory, 2010).

Theorists have suggested that biased processing of emotional stimuli may serve as a key mechanism not only in the development and maintenance of psychopathology but also in the intergenerational transmission of risk. Specifically, although it is clear that both genetic and environmental influences contribute to the development of psychopathology, theorists have proposed that biases in the processing of emotional stimuli may serve as a final common pathway for these influences in the intergenerational transmission of psychopathology (e.g., Goodman & Gotlib, 1999). Within this context, theorists have proposed that children of depressed mothers would be predicted to exhibit biased processing only for depression-relevant information, whereas children

of anxious mothers would be expected to exhibit biased processing only for threat-relevant information. There is growing evidence for this type of specificity. For example, there is evidence that children of depressed mothers exhibit attentional biases specifically to sad faces (e.g., Gibb, Benas, Grassia, & McGeay, 2009), whereas children of anxious mothers exhibit attentional biases to threat-relevant stimuli (Mogg, Wilson, Hayward, Cunning, & Bradley, 2012). Importantly, these biases appear to be at least partially independent of the children's current symptoms or history of diagnoses, suggesting that they are not simply correlates or consequences of psychopathology in the children and may be true vulnerability factors.

Information-processing biases such as attentional biases are driven by dysregulation in corticolimbic circuitry in which heightened amygdala reactivity is not effectively downregulated by prefrontal areas (e.g., Disner, Beevers, Haigh, & Beck, 2011). However, no study of which we are aware has formally examined whether children of depressed or anxious parents exhibit experience-specific patterns of neural reactivity. The goal of this study was to fill this gap in the literature. In doing so, we focused on children's pupil dilation. Pupils become dilated in response to stimuli that require greater cognitive load or that have greater emotional intensity (e.g., Siegle, Steinhauer, Carter, Ramel, & Thase, 2003). Research shows that the pupil increases in dilation as limbic regions such as the amygdala (e.g., Siegle, Steinhauer, Stenger, Konecky, & Carter, 2003) and the midbrain reticular formation (e.g., Beatty, 1986) become stimulated. Studies using pupillometry and fMRI concurrently suggest that pupil dilation provides a summative index of

Conflicts of interest statement: No conflicts declared.

task-relative cognitive and affective brain activity (Siegle, Steinhauer, Stenger, et al., 2003).

There is growing evidence that depressed adults exhibit greater pupil dilation to negative emotional words compared with never depressed adults (e.g., Siegle, Granholm, Ingram, & Matt, 2001; Siegle, Steinhauer, Carter, et al., 2003). We should note that, however, the one study conducted to date with currently depressed youth found that they exhibited less pupil dilation in response to negative words than did never depressed youth (Silk et al., 2007). With regard to anxiety, one recent study found that anxious youth exhibited increased sustained pupil dilation in response to fearful faces compared with nonanxious youth (Price et al., 2013). However, no study of which we are aware has examined pupillary reactivity as an index of biased processing of emotional information in children of depressed or anxious parents. The identification of physiological factors (i.e., pupillary differences to emotional stimuli) associated with risk for MDD may aid clinicians and researchers in objectively identifying specific markers of risk early on in development, even in the absence of overt behavioral signs.

The goal of this study, therefore, was to examine the links between mothers' history of major depressive disorder (MDD) and/or anxiety disorders and children's pupillary reactivity to facial displays of emotion. We predicted that children of depressed, compared with nondepressed, mothers would exhibit differences in pupil dilation specifically to sad, but not happy or angry, faces. Consistent with the majority of past research with depressed adults, we predicted that children of mothers with a history of MDD during the child's life would exhibit greater pupil dilation to sad faces. Second, we predicted that children of mothers with a history of anxiety disorders would exhibit increased pupil dilation to angry, but not happy or sad, faces. To provide a stronger test of our hypotheses, we also evaluated the impact of emotional intensity on children's pupillary reactivity. Specifically, we morphed the facial images from neutral to full emotion. Consistent with prior research demonstrating that increasing intensity of sad facial expressions is associated with enhanced activity in the left amygdala (Blair, Morris, Frith, Perrett, & Dolan, 1999), we predicted that pupil dilation would track the intensity of the expressions, such that it would be greatest at the highest morph level (full emotion).

Method

Participants

Potential participants were recruited from the community through a variety of means (e.g., newspaper and bus ads, flyers). Mothers responding to the recruitment advertisements were initially screened over the phone to determine potential eligibility. Those reporting either significant depressive symptoms during the child's life or no significant lifetime symptoms of

depression were invited to participate in the study. Participants in this study were 117 mothers and their children drawn from the community. To qualify for inclusion in the 'depressed' group ($n = 53$), mothers were required to meet criteria for MDD during the child's lifetime according to the *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV)* (American Psychiatric Association, 1994). To qualify for inclusion in the 'nondepressed' group ($n = 64$), mothers were required to have no lifetime diagnosis of any *DSM-IV* mood disorder and no current Axis I disorder. Of these participants, 25 (23 from the depressed group) also had a history of one or more anxiety disorders during their child's lifetime (social phobia = 12, generalized anxiety disorder = 1, posttraumatic stress disorder = 6, panic disorder = 7, obsessive-compulsive disorder = 3). Exclusion criteria for all of the mothers in the study included symptoms of schizophrenia, organic mental disorder, alcohol or substance dependence within the last 6 months, or history of bipolar disorder. The average age of mothers in our sample was 40.97 years ($SD = 6.59$, Range = 26–55) and 87% were Caucasian. The median family income was \$55,000–60,000 and, in terms of education level, 43% of the mothers had graduated from college. For the children in our sample, the average age was 11.18 years (Range = 8–14; $SD = 1.89$), 47% were girls, and 83% were Caucasian.¹

Measures

The Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1995) and the Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (K-SADS-PL; Kaufman, Birmaher, Brent, & Rao, 1997) were used to assess for current *DSM-IV* Axis I disorders in mothers and their children, respectively. Two separate trained interviewers administered the SCID-I and the K-SADS-PL to mothers and children, respectively. As noted above, 53 mothers met criteria for MDD during their child's life (16 met criteria for current MDD). Twenty-five mothers had a history of an anxiety disorder (23 from the MDD group). In terms of children's diagnoses, five met criteria for a lifetime episode of MDD (all were children of mothers with a history of MDD themselves), of whom one met criteria for current MDD. Eleven children met criteria for a lifetime episode of one or more anxiety disorders (six whose mother had an anxiety diagnosis), eight of whom met criteria one or more current anxiety diagnoses. To assess interrater reliability, a subset of 20 SCID and K-SADS interviews from this project were coded by a second interviewer and kappa coefficients for diagnoses of MDD and anxiety disorders in mothers and children were excellent (all κ s = 1.00).

Children's symptoms of depression and anxiety were assessed using the Children's Depression Inventory (CDI; Kovacs, 1981) and the Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997), respectively. In this study, both the CDI and the MASC exhibited good internal consistency ($\alpha = .86$ and $\alpha = .86$, respectively).

Children's levels of pubertal development were assessed using the Sexual Maturation Scale (SMS; Marshall & Tanner, 1969, 1970). The SMS consists of drawings of the five Tanner stages of pubertal development with separate drawings available for girls and boys. Written descriptions are provided for each stage and the respondent is asked to indicate which stage best represents the current level of pubertal development. Consistent with past research examining affective aspects of pubertal development (e.g., Forbes, Williamson, Ryan, & Dahl, 2004), participants were classified as prepubertal if they were in Tanner stages 1 or 2, and as pubertal/postpubertal if they were in Tanner stages 3, 4, or 5.

Pupil dilation was assessed in a moderately lit room using Tobii T60 & T60XL eye-trackers, while participants viewed

facial displays of emotion. The stimulus set consists of full-color pictures of actors taken from a standardized stimulus set (Matsumoto & Ekman, 1988) displaying a variety of emotions (e.g., sad, happy, angry, neutral). The stimuli consisted of emotional and neutral photographs from each actor, morphed to form a continuum of 10% increments between the two photographs. Each emotion is represented by four continua (two male and two female actors), for a total of 12 continua. Eleven morphed images were used from each continuum, representing 10% increments of the two emotions ranging from 100% neutral (0% target emotion) to 100% target emotion (e.g., 90% Neutral, 10% Sad; 80% Neutral, 20% Sad; and so on). The pictures were presented, one at a time in the middle of the screen for a duration of 3 s, in random order in two blocks and the participant was asked to indicate which emotion was being presented (sad, happy, angry, neutral). To provide an adequate number of trials for pupillary analyses within each morph level, images were binned into three separate morph conditions for analyses: low (10%, 20%, and 30%), medium (40%, 50%, 60%, and 70%), and high (80%, 90%, and 100%).

During this task, pupil size was recorded using the eye-trackers at 60 Hz (every 16.7 ms) for 3 s following the onset of each facial stimulus. Data were cleaned using Siegle et al. (2001), Siegle, Steinhauer, Carter, et al. (2003) standard procedures derived from Granholm, Asarnow, Sarkin, and Dykes (1996). Trials comprised of over 50% blinks were removed from consideration. Linear interpolations replaced blinks throughout the data set and data were smoothed using a 10-point weighted average filter. Effects associated with a light-reflex that were independent of stimulus type were removed by subtracting the mean waveform across all three valences from the average waveform for each valence (Franzen, Buysee, Dahl, Thompson, & Siegle, 2009). Data were resampled to 3 Hz (one sample every 333 ms) to allow inspection of independent features of pupillary motility above and beyond the high level of autocorrelation in the smooth pupil waveform. The average pupil diameter over the 333 ms preceding the onset of the stimulus was subtracted from pupil diameter after stimulus onset to produce stimulus-related pupil dilation waveforms.

Results

As shown in Table 1, there were no significant differences between children of depressed versus nondepressed mothers in terms of age or gender. However, the children of depressed mothers were more likely to come from minority backgrounds and have lower family incomes than children of nondepressed mothers. This said that there were no racial/ethnic group or family income differences in pupil dilation and the significant results reported below were maintained even after statistically controlling for the influence of these variables.

As a first step in our analyses, we tested for group differences in behavioral accuracy of detecting emotions. To do this, we conducted a 2 (Mom MDD: no, yes) \times 2 (Mom Anxiety: no, yes) \times 3 (Target Emotion: angry, happy, sad) \times 3 (Morph Level: low, medium, high) repeated measures ANOVA, with proportion of faces correctly identified per level of morph serving as the dependent variable. Results indicated significant main effects for emotion ($F(2, 112) = 58.09, p < .001, \eta_p^2 = .51$) and morph level ($F(2, 112) = 345.37, p < .001, \eta_p^2 = .86$). However, none of the other analyses was significant (lowest $p = .09$). As expected,

Table 1 Demographic characteristics of participants

	Low risk (<i>n</i> = 57)	High risk (<i>n</i> = 67)	<i>t</i> / χ^2
Sex	55	50	.34
(% Female)			
Ethnicity	61	40	6.38*
(% White)			
Age			
<i>M</i>	11.12	11.15	.09
<i>SD</i>	1.75	2.08	
Family income			
Median	\$60,000–\$65,000	\$40,000–\$45,000	3.52**

Low risk = children of nondepressed mothers; High risk = children of depressed mothers.

* $p < .01$, ** $p < .001$.

there was a general linear increase in the proportion of faces endorsed as sad, happy, and angry from low ($M = .31$) to the medium ($M = .69$) to the high ($M = .90$) morph levels. Examining the main effect of emotion, youth were better at detecting happy faces ($M = .82$), compared with angry ($M = .56$) or sad ($M = .53$) faces, among all morph levels.

Next, we tested for differences in pupil dilation using linear mixed modeling with an autoregressive (AR1) covariance structure. Data were included for the mean pupil dilation during each 333 millisecond epoch for each emotion at each morph level per subject, with subject treated as a random effect and time, morph, and emotion treated as repeated measures. We first tested for potential pubertal and gender differences in pupil dilation to the emotional stimuli. Predictors in this analysis were pubertal status, gender, emotion, morph, time, and all interactions were entered as fixed effects. We found evidence for significant puberty \times morph ($F_{(2, 6401)} = 7.13, p < .01$) and puberty \times emotion ($F_{(2, 6299)} = 13.34, p < .001$) interactions.² None of the other analyses with pubertal status or child sex were significant (lowest $p = .07$). Examining the form of the pubertal status \times morph interaction, we tested for puberty differences separately among each morph condition. The pubertal status main effect was significant for the high morph condition ($F_{(1, 1258)} = 8.97, p < .01$), but not among the low or medium morph conditions (lowest $p = .07$). At the highest morph level, postpubertal youth exhibited greater pupil dilation to all emotional faces ($M = .024, SE = .001$) than prepubertal youth ($M = .019, SE = .001$). Next, we examined the form of the pubertal status \times emotion interaction by conducting analyses separate among the three emotion conditions. Results indicated a significant pubertal status main effect for the sad condition ($F_{(1, 1007)} = 17.85, p < .001$), but not for the angry or happy conditions (lowest $p = .07$). Results indicated that the prepubertal youth exhibited increased pupil dilation to sad faces across all morph conditions ($M = .06, SE = .001$) compared with postpubertal youth ($M = .05, SE = .001$).

Following this, we examined the effects of mothers' MDD and anxiety diagnoses on children's pupillary reactivity to emotional stimuli. Specifically, we conducted a 2 (Mom MDD: yes, no) \times 2 (Mom Anxiety: yes, no) \times 3 (Emotion: angry, happy, sad) \times 3 (Morph Level: low, medium, high) \times 10 (Time: sampled every 333 ms for 3 s after the onset of stimulus) linear mixed model with pupil dilation serving as the dependent variable and child pubertal status included as a covariate to account for pubertal differences in pupillary reactivity.³ Results of these analyses are presented in Table 2. Focusing on the highest order interactions that were significant,⁴ We first examined the significant Mom MDD \times Emotion \times Morph interaction by conducting follow-up analyses within each morph level. Results indicated a significant Mom MDD \times Emotion interaction for the low ($F_{(2, 2272)} = 4.55$; $p = .02$), medium ($F_{(2, 2607)} = 8.82$; $p < .001$), and high ($F_{(2, 2279)} = 11.56$; $p < .001$) morph conditions. Analyses were then conducted separately for each emotion condition at the low, medium, and high morph levels. At the low and medium morph levels, the main effect of Mom MDD was not significant among any of the separate emotion conditions (lowest $p = .98$). Focusing on the highest morph level, results indicated a significant main effect of Mom MDD for the sad condition ($F_{(1, 157)} = 4.19$, $p = .04$), but not for the happy ($F_{(1, 171)} = 1.30$, $p = .26$) or angry ($F_{(1, 143)} = .46$, $p = .50$) conditions. As shown in Figure 1, children of depressed mothers exhibited greater pupil dilation to sad faces ($M = .053$,

Table 2 Linear mixed modeling results

	F
Time	1.26
Emotion	527.67***
Morph	42.81***
Pubertal Status	0.31
Mom MDD	1.67
Mom Anxiety	0.19
Time \times Emotion	38.69***
Time \times Morph	9.50***
Time \times Mom MDD	0.45
Time \times Mom Anxiety	0.22
Emotion \times Morph	30.39***
Emotion \times Mom MDD	3.12
Emotion \times Mom Anxiety	18.78***
Morph \times Mom MDD	2.08
Morph \times Mom Anxiety	4.81**
Time \times Emotion \times Morph	2.22***
Time \times Emotion \times Mom MDD	0.96
Time \times Emotion \times Mom Anxiety	0.67
Time \times Morph \times Mom MDD	0.96
Time \times Morph \times Mom Anxiety	0.66
Emotion \times Morph \times Mom MDD	11.30***
Emotion \times Morph \times Mom Anxiety	2.31*
Time \times Emotion \times Morph \times Mom MDD	0.89
Time \times Emotion \times Morph \times Mom Anxiety	1.00

MDD, major depressive disorder.

* $p < .05$, ** $p < .01$, *** $p < .001$.

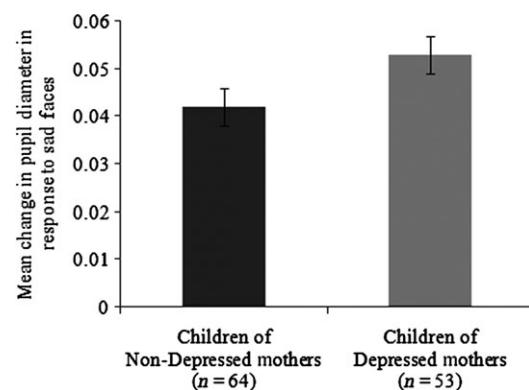


Figure 1 Differences in average pupil dilation to sad faces between children of depressed and nondepressed mothers at the highest morph level

$SE = .004$), compared with children of nondepressed mothers ($M = .042$, $SE = .004$). Focusing next on the Mom Anxiety \times Emotion \times Morph interaction, we conducted follow-up analyses for each of the separate morph conditions. The Mom Anxiety \times Emotion interaction was significant among the medium ($F_{(2, 2601)} = 8.93$, $p < .001$) and high ($F_{(2, 2265)} = 9.01$, $p < .001$) morph levels, but not among the low morph level ($F_{(2, 2268)} = 2.92$, $p = .06$). We then conducted separate analyses for each of the separate emotion conditions. At the medium morph level, the main effect of Mom Anxiety was not significant among any of the separate emotion conditions (lowest $p = .17$). However, at the highest morph level, results indicated a significant main effect of Mom Anxiety for the angry condition ($F_{(1, 143)} = 4.87$, $p = .03$). As shown in Figure 2, children of anxious mothers exhibited greater pupil dilation to angry faces ($M = .027$, $SE = .006$) compared with children of nonanxious mothers ($M = .011$, $SE = .003$). The main effect of Mom Anxiety was not significant among the sad or happy conditions (highest $p = .44$).

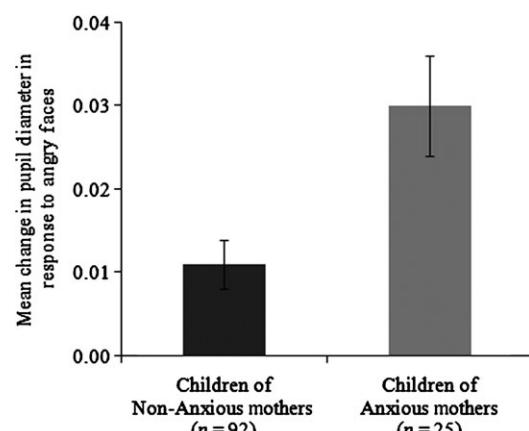


Figure 2 Differences in average pupil dilation to angry faces between children of anxious and nonanxious mothers at the highest morph level

We then evaluated the robustness of these effects to determine whether they would be maintained after statistically controlling for mother's current symptoms of depression and anxiety and for children's current symptoms and lifetime diagnoses of depression and anxiety. Focusing first on the link between Mom MDD and children's pupillary reactivity to sad faces, this effect was maintained even after statistically controlling for mother's current symptoms of depression ($F_{(1, 157)} = 4.85; p = .03$). It was also maintained after statistically controlling for children's current symptoms of depression and after excluding children with a lifetime history of MDD (highest $p = .04$). These results suggest that the increased physiological reactivity observed in children of depressed mothers was at least partially independent of the mothers' current levels of depression and is not simply a correlate or consequence of children's own current or past history of depression. Focusing next on the link between Mom Anxiety and children's pupillary reactivity to angry faces, this effect was maintained after statistically controlling for mother's current symptoms of anxiety ($F_{(1, 149)} = 6.63; p = .01$). However, it was reduced to a nonsignificant trend when statistically controlling for children's current symptoms of anxiety ($F_{(1, 142)} = 3.71; p = .06$) and when excluding children with a lifetime history of an anxiety disorder ($F_{(1, 126)} = 3.53; p = .06$).

Discussion

The primary goal of this study was to examine physiological indices of emotion processing in children of depressed and anxious mothers. Consistent with our hypothesis, we found that children of mothers with a history of MDD during their lifetime exhibited greater pupil dilation specifically to sad, but not angry or happy, faces compared with children of mothers with no history of depression. In addition, children of mothers with a history of one or more anxiety disorders during their lifetime exhibited increased pupil dilation specifically to angry faces. As predicted, these patterns of reactivity were greater at higher levels of emotional intensity (morph level), which is consistent with prior research demonstrating that increasing intensity of sad facial expressions is associated with enhanced activity in the left amygdala (Blair et al., 1999). Importantly, the link between maternal MDD and children's reactivity to sad facial expressions was maintained even after statistically controlling for mothers' and children's current levels of depressive symptoms and after excluding mother-child pairs in which the child had a history of MDD. In combination, these results suggest that children's greater reactivity to sad facial expressions was not simply a correlate or consequence of their own depression. This suggests that pupil dilation may represent a promising biomarker of

risk in children of depressed parents. A similar pattern of findings was observed regarding the link between mothers' history of anxiety disorders and children's pupil dilation to angry faces, although the relation was reduced to a nonsignificant trend ($p = .06$) after statistically controlling for the influence of children's current symptoms of anxiety or their past history of anxiety disorders.

To our knowledge, this is the first study to examine pupil dilation differences to sad, angry, and happy faces among children of depressed and anxious mothers. Importantly, these findings parallel the attentional biases literature, which has found that children of depressed mothers exhibit attentional biases specifically to sad faces (e.g., Gibb et al., 2009), whereas children of anxious mothers exhibit attentional biases for threat-relevant stimuli (Mogg et al., 2012). The current findings suggest a physiological mechanism underlying attentional biases in at-risk kids – disruptions in the corticolimbic circuit – that has been shown to underlie attentional biases in currently disordered adults.

This said that there are several potential brain mechanisms within this circuit that might underlie this increased initial pupillary response to sad and angry faces. As discussed earlier, pupillary reactivity has been related to stimulation of the amygdala (e.g., Siegle, Steinhauer, Stenger, et al., 2003) and stimulation of the frontal cortex and anterior cingulate cortex via connections from the midbrain reticular formation (e.g., Beatty, 1986). This increased initial pupil dilation to sad and angry faces shown in children of depressed and anxious mothers, respectively, could indicate increased limbic reactivity or increased engagement of regulatory structures. Pupillometry, therefore, cannot distinguish between purely emotional reactions and other processes, such as emotion regulation, that also involve cognitive components (Urry et al., 2006). This said that a recent study found that daughters of depressed mothers exhibit an increased amygdala response in the presence of negative emotional information (Joormann, Cooney, Henry, & Gotlib, 2012), supporting the role of increased limbic activation in children of depressed mothers, a neural abnormality that appears to precede the onset of a depressive episode. To more definitively delineate the neural mechanisms underlying high-risk children's processing of emotional faces, studies are needed that incorporate both pupillometry and neuroimaging.

We should highlight an additional finding from this study. We found that postpubertal children exhibited increased pupil dilation to faces at the highest morph level compared with prepubertal children, regardless of emotion type. These findings are similar to the Silk et al. (2009) study demonstrating that postpubertal youth exhibit increased pupil dilation to emotional words, regardless of valence, compared with prepubertal youth. This

finding is consistent with models suggesting that puberty is associated with greater reactivity of neurobehavioral systems involved in emotional information processing (Steinberg et al., 2006).

This study benefited from a number of strengths including the use of diagnostic interviews to confirm mothers' and children's history of psychopathology, the large sample size, and the focus on evaluating specificity in the link between maternal psychopathology and children's processing of emotional stimuli. The study is also the first to utilize pupillometry to assess biases in the processing of emotional stimuli in children of depressed and anxious mothers. As such, it suggests that this may be a promising approach to better understanding the physiological mechanisms underlying children's information-processing biases. This said that there were also a number of limitations as well, which point toward future avenues of research. First, we used a retrospective, cross-sectional design for our study, which does not allow us to draw causal conclusions. Future research is needed, therefore, to determine whether maternal depression or anxiety actually predicts prospective changes in children's pupillary reactivity to emotional stimuli. Future research is also needed to determine whether pupil dilation predicts onset of depression and anxiety diagnoses. Second, the mechanisms involved in the intergenerational transmission of psychopathology include genetic and environmental influences. Indeed, several genes linked to depression risk are associated with disruptions in corticolimbic circuitry. Specifically, variation in a functional polymorphism (5-HTTLPR) in the serotonin transporter gene (*SLC6A4*) is linked to greater amygdala activation, reduced functional connectivity between the amygdala and prefrontal regions, and attentional biases for emotional stimuli (for a review, see Gibb, Beevers, & McGeary, 2013). Future research is needed to more carefully delineate the specific genetic and environmental influences on children's information-processing biases. Third, as previously described, although pupillometry is a useful tool for measuring emotional reactivity, the lack of neural specificity is a limitation to the pupillometry approach. Future research could address this problem using concurrent collection of pupillometric and neuroimaging data, which are now available in many fMRI environments. Fourth, our task only allowed us to examine differences in pupillary reactivity within the first 3 s following stimulus onset. However, other research has suggested that pupillary reactivity differences in depressed and anxious populations persist well after the stimulus has disappeared from the screen, indicating an emotional ruminative response (e.g., Price et al., 2013; Siegle, Steinhauer, Carter, et al.,

2003). Future research is needed to also examine if sustained emotional processing differences exist between children of depressed versus nondepressed mothers and between children of anxious versus non-anxious mothers. Next, we did not observe a clear step function in children's pupillary reactivity as a function of morph level. This may have been due to the limited number of trials included at each morph level, which required us to collapse these levels into broader groups of low, medium, and high morph. Future research should seek to include a larger number of trials, so that the full morph continuum can be analyzed. It is also important to note that the majority of anxious mothers in the current sample also had a prior history of MDD. Therefore, additional studies are needed to determine whether children of mothers with a history of an anxiety disorder without comorbid MDD exhibit increased pupil dilation to angry faces. Finally, we utilized angry faces as the threat-relevant stimuli in this study. However, other researchers have used fearful faces or a combination of angry and fearful. To the extent that the development of information-processing biases in children is due to direct exposure to parents' facial displays of emotion, the use of fearful faces may provide greater power to detect such effects. Future research is needed to test this possibility.

In summary, the current findings add to the growing body of research suggesting that differences in physiological reactivity to depression- and anxiety-relevant cues may represent an important mechanism in the intergenerational transmission of depression and anxiety. Although prospective studies are needed to more formally evaluate the causal role of this differential reactivity on children's risk for depression and anxiety onset (cf. Gibb et al., 2009), this differential affective response appears to be a promising biomarker of risk and a potentially useful target for preventive interventions designed to reduce depression and anxiety risk among these high-risk groups.

Acknowledgements

This project was supported by grants HD057066 (NICHD) and MH098060 (NIMH) awarded to B.E.G. at Binghamton University (SUNY).

The authors thank Ashley Johnson, Lindsey Stone, Andrea Hanley, Mary Woody, Sydney Meadows, and Michael Van Wie for their help in conducting assessments for this project.

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Key points

- Children of depressed and anxious mothers are at heightened risk for depression and anxiety disorders, respectively, suggesting the importance of identifying factors implicated in this risk.
- This study examined differences in physiological reactivity to emotional faces among children at high and low familial risk for depression and anxiety.
- We found that children of mothers with a history of major depression (MDD) exhibited increased pupil dilation, a measure of physiological reactivity, to sad faces and children of anxious mothers exhibited increased pupil dilation to angry faces.
- Differences in physiological reactivity to depression- and anxiety-relevant cues may represent an important mechanism in the intergenerational transmission of depression and anxiety.

Notes

¹Twenty-seven children in this study were on current medications (psychotropic medication = 6; asthma or allergy medications = 16; other medication = 6). Importantly, pupil dilation was not significantly related to medication status (lowest $p = .83$) and all of the main findings were maintained even after entering medication status as a covariate in the analyses (highest $p = .04$).

²Importantly, the pubertal findings were maintained even after statistically controlling for children's age (highest $p = .02$).

³This study was unable to examine the Mom MDD \times Mom Anxiety interactions (i.e., comorbid influences) due to small cell sizes. Specifically, there were only two youth whose mother had a history of anxiety and no prior history of MDD.

details of the other lower order interactions described in Table 2 can be provided by the author upon request.

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Accepted for publication: 7 February 2014

Published online: 17 March 2014