Emotion processing in infancy: Specificity in risk for social anxiety and associations with two-year outcomes

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Abstract

The current study examined the specificity of patterns of responding to high and low intensity negative emotional expressions to infants of mothers with social phobia, and their association with child outcomes at two years of age. Infants of mothers with social phobia, generalised anxiety disorder (GAD) or no history of anxiety were shown pairs of angry and fearful emotional expressions at 10 weeks of age. Symptoms of social withdrawal, anxiety and sleep problems were assessed at two years of age. Only infants of mothers with social phobia showed a tendency to look away from high intensity fear faces; however infants of mothers with both social phobia and GAD showed a bias towards high intensity angry faces. Among the offspring of mothers with social phobia, anxiety symptoms at two years of age were associated with a preference for high intensity fear faces in infancy. The reverse pattern was found amongst the offspring of non-anxious mothers. These findings suggest a possible specific response to emotional expressions among the children of mothers with social phobia.

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Introduction

Social phobia is a chronic, disabling disorder, characterised by intense fear of negative evaluation by others, that affects between 7 and 13% of Western populations (Furmark, 2002). Adults and children with high levels of social anxiety have been shown to evidence distinctive patterns of responding to negative emotional faces (e.g. Bögels & Mansell, 2004; Garner, 2010). It remains unclear, however, whether responses to social emotional information have a specific role in the aetiology of social anxiety. Tentative support comes from our previous report of responses to emotional faces amongst 10 week old infants of mothers with social phobia. We found that, whereas 10 week old infants of non-anxious mothers showed increased initial orientation and overall looking to high, versus low, fear faces, infants of mothers with social phobia showed the reverse pattern (Creswell et al., 2008). The purpose of this study is to extend these findings to address the following questions: (i) is this pattern of responding to emotional faces specific to infant offspring of mothers with social phobia, in comparison to offspring of mothers with another anxiety disorder (here, Generalised Anxiety Disorder (GAD)), and (ii) is infant response style to emotional faces associated with later anxiety symptoms, assessed here at 2 years of age.

Responses to emotional expressions: role in the development of anxiety

A number of studies have demonstrated that socially anxious individuals show distinctive attentional responses to emotional faces (e.g. Bögels & Mansell, 2004), which appear to reflect a heightened sensitivity to potentially threatening faces at early stages of processing. For example, compared to non-anxious controls, socially anxious adults have been found to identify angry faces at lower levels of intensity (Joorman & Gotlib, 2006). There is increasing support for the idea that this initial sensitivity, or hypervigilance, is followed by avoidance, which is viewed as an attempt to reduce discomfort associated with the stressful stimuli (e.g. Mogg, Bradley, de Bono, & Painter, 1997). In turn, this avoidance leads to heightened potentiation of the fear response and reduced habituation, thereby maintaining the fear response (Mogg & Bradley, 1998).

There is a well established familial basis to the development of social phobia (e.g. Lieb et al., 2000; Mancini, van Ameringen, Szatmari, Fugere, & Boyle, 2006); from a meta-analysis of twin studies a heritability estimate of .65 was estimated for social anxiety (Beatty, Heisel, Hall, Levine, & La France, 2002), although many studies suggest a more modest effect (e.g. 0.31 - Kendlar et al., 1992). It is

> **Comment [CE2]:** Should the unit of measurement be stated?

72 important to note, however, that most studies have suggested that much of the inherited component is
73 common across anxiety and depressive disorders (Andrews, 1996; Eley, 1999), although Kendlar,
74 Myers, Prescott, and Neale (2001) concluded that 13% of the variance in social anxiety was accounted
75 for by specific genetic factors. The phenotypic expression of this genetic risk is of much interest, and
76 candidates that have been considered have focused on temperamental characteristics, such as
77 behavioural inhibition (BI; Elizabeth et al., 2006), neuroticism, introversion (Bienvenu, Hettema, Neale,
78 Prescott, & Kendlar, 2007) and harm avoidance (Lochner et al., 2007). Theories of the role of social
79 information processing, have also suggested that individual cognitive biases may be an integral part of,
80 and a risk factor for, social anxiety (Richards, French, Nash, Hadwin, & Donnelly, 2007); this proposition
81 has been labelled the 'integral hypothesis', and can be contrasted with two competing hypotheses,
82 namely, the 'inferred bias hypothesis' (McClure & Nowicki, 2001; Richards et al., 2007) and the 'inhibition
83 hypothesis' (Kindt & van den Hout, 2001). The 'inferred bias hypothesis' suggests that social anxiety
84 may itself interfere with social information processing, leading to the expectation that social information
85 processing biases should increase with age, and are unlikely to be apparent in early infancy. The
86 'inhibition hypothesis' suggests, by contrast, that a bias for threatening stimuli is normal in young
87 children, but becomes inhibited in non-anxious children through development. Support for the 'integral
88 hypothesis' comes from two studies to date. First, Joorman, Talbot, and Gotlib (2007) used a dot-probe
89 paradigm and presented sad-neutral and happy-neutral face pairs to 21 daughters (aged 9 to 14 years)
90 of mothers with a history of depression (the 'high risk' group) and 20 daughters of mothers with no
91 history of an Axis I disorder (the 'low risk' group). High, but not low, risk daughters selectively attended to
92 sad faces, whereas the reverse pattern was found for happy faces. While these findings may have been
93 a result of environmental influence, it is notable that they were not attributable to *current* symptoms of
94 depression (or anxiety), and, as such, go against the 'inferred bias' hypothesis. In relation to anxiety and
95 threat faces, we reported preliminary support for the 'integral bias hypothesis' from a study of looking
96 responses of infant offspring of mothers with social phobia and non-anxious mothers assessed at 10 and
97 16 weeks and 10 months of age. We were interested in infants' responses to high versus low intensity
98 emotional faces, based on findings with adults that suggest that high levels of social anxiety are
99 associated with avoidance of extreme positive and negative (but not neutral) emotional expressions,
100 under conditions of socially-evaluative threat (Mansell, Clark, Ehlers, & Chen, 1999). Infants were
101 presented with a series of pairs of morphed faces, in which one face represented 50% emotional
102 expression (of either happiness, fear or anger) while the other represented a high (75% or 100%) or low
103 (0% or 25%) intensity version. Although there was no direct examination of the impact of social threat, all
104 conditions involved the infant being confronted with emotional faces facing directly towards them. Infants
105 of non-anxious mothers, at 10 weeks and 10 months, were more likely to initially orient to high (vs. low)
106 intensity fear faces, when presented to the right of a control (50%) expression and they showed
107 increased overall looking to the high intensity fear face. In contrast, 10 week and 10 month infants of
108 mothers with social phobia were more likely to look initially to the low intensity fear faces and show
109 increased overall looking to the low intensity fear face (Creswell et al., 2008). Thus, while we found no
110 evidence for initial hypervigilance to threat faces, the results were consistent with a tendency for infants
111 at genetic risk of social phobia to avoid high intensity emotional expressions. Conclusions must remain
112 tentative however, as although the infants were very young, at 10 weeks they have still had substantial
113 social experience (although it was notable that responses to fear faces were not associated with
114 measures of maternal social behaviour). In addition, it could not be established whether infant responses
115 to emotional expressions are specifically associated with maternal social phobia, as opposed to other
116 maternal anxiety disorders. Furthermore, since no longer-term outcomes were considered, it could not
117 be established whether infant responses to emotional faces are a precursor to longer term anxiety
118 symptoms.

Responses to emotional expressions: specificity to social anxiety

While evidence from non-clinical populations suggests that there is an emotion-congruent effect, in which particular patterns of hypervigilance- avoidance to emotional stimuli are associated with anxious versus depressive symptoms (e.g. Bradley, Mogg, & Lee, 1997; Bradley, Mogg, Falla, & Hamilton, 1998), it is less clear whether there is such specificity between anxiety subtypes. For example, a lack of specificity is suggested by findings that hypervigilance to threat related faces (anger and/or fear) is associated with the presence of both social phobia (e.g. Mogg, Bradley, Miles, & Dixon, 2004) and GAD (e.g. Bradley, Mogg, White, Groom, & de Bono, 1999). However, support for disorder-specific processing of emotional material in social anxiety comes from evidence that both hypervigilance (Mogg & Bradley, 2002) and subsequent avoidance (e.g. Garner, Mogg, & Bradley, 2006) are significantly associated with social anxiety after controlling for trait anxiety (Bögels & Mansell, 2004).

Few studies have examined associations between responses to emotional expressions and social anxiety in children. Those that have done so provide support for differential attentional responding among highly anxious vs. non-anxious children (all to date using dot-probe methodologies); however, the issue of anxiety subtype specificity is unresolved. Stirling, Eley, and Clark (2006) presented 79 children (8-11 years) from a community population with negative (fearful and angry), neutral and positive faces within a dot-probe paradigm. In this study, stimuli were presented for a relatively long duration (1000 ms), preventing conclusions being drawn about rapid attentional responses to emotional stimuli; nevertheless, over this longer period, avoidance of negative facial expressions was found to be associated with child self-reported social anxiety, but not general anxiety- i.e. findings consistent with an emotion-congruent account. In contrast, a number of other studies have failed to find such evidence. Thus, Monk et al. (2006) presented adolescents with GAD (age 9-17 years) with angry/neutral face pairs, again for a relatively long duration (500 ms) and also found that the clinical group showed avoidance of negative (angry) faces. Furthermore, in a subsequent study in which stimuli were presented over a shorter duration (17 ms), adolescents with GAD showed an initial attentional bias towards angry faces (Monk et al., 2008). Hypervigilance for angry faces was also found among more severe, but not milder, cases of GAD in children aged 7 to 12 years (Waters, Mogg, Bradley, & Pine, 2008). In a study of 101 children with mixed anxiety disorders and 51 non-anxious control children, Roy et al. (2008) reported that while the clinical group showed a bias towards angry (but not happy) faces, there were no significant associations with specific anxiety diagnoses. In sum, although overall conclusions that can be drawn are limited by the different age-ranges of participants, and differences in experimental methods (e.g. different lengths of time for the presentation of stimuli, and inclusion of different types of emotional expressions), the balance of evidence provides only limited support for specificity of responses to emotional expressions amongst children according to particular anxiety subtypes.

The current study aimed to extend our previous research, first, by determining whether the biases found in responding to emotional expressions were specific to those offspring at risk of social phobia, by comparing them to a group of offspring with a more general risk of anxiety (i.e. offspring of mothers with GAD), as well as differing from offspring of non-anxious, control, mothers. While dot probe methods are clearly not directly applicable with infant samples, numerous studies have assessed infant attentional responses by recording patterns of infant looking to different stimuli (see Creswell et al., 2008). Specifically, because social anxiety is associated with avoidance of extreme emotional expressions, even when positive, under conditions of socially-evaluative threat (Mansell et al., 1999), we examined infant responses to extreme emotional expressions in comparison to moderate expressions. Following on from our previous report, we have focused here on responses of 10 week old infants, as it was at this age that the clearest effects of maternal social phobia were found. In our previous report we considered infant looking responses to angry, fearful and happy faces, and found significant effects only for fearful

165 faces. We have accordingly followed this up with further consideration of fearful faces, but we have also
166 continued to examine responses to angry faces, because findings of previous studies with anxious
167 children have most consistently reported differential responding to angry faces. Finally, whereas in our
168 previous report the index group included offspring of mothers with social phobia and comorbid GAD, as
169 the current study is concerned with specificity, only the offspring of mothers with pure social phobia (i.e.
170 social phobia in the absence of GAD) were included, along with a new sample of offspring of mothers
171 with pure GAD (i.e. GAD in the absence of social phobia) were included, as well as mothers with no
172 history of an anxiety disorder. The first hypothesis, therefore, set out to replicate our previous findings
173 but restricting the sample to the pure social phobia group. The initial hypotheses are as follows:

174 1. In comparison to infants of mothers with no history of anxiety, 10 week old infants of mothers with
175   social phobia will show reduced looking to high intensity negative emotional faces (vs. low intensity
176   faces) when presented alongside a face of moderate intensity as indexed by looking times and initial
177   orientation to stimuli.
178 2. Biases in responding to high vs. low intensity faces will be specific to infants of mothers with Social
179   Phobia, in comparison to infants of mothers with GAD

180 We also aimed to examine whether infant looking responses to emotional faces were associated with
181 later anxiety symptoms. We assessed symptoms of social and general anxiety when the children were
182 two years of age, as behaviours indicative of strong social fears, that predict an increased incidence of
183 social phobia in later life, have been identified in children as young as 21 months of age (Rosenbaum et
184 al., 1992). We hypothesised as follows:

185 3. Responses to high/low intensity negative faces at 10 weeks will be associated with children's
186   outcomes at 2 years of age.

187 The outcomes we considered were social anxiety problems (based on social withdrawal), general
188 anxiety problems and also sleep problems. Sleep problems were included as recent findings suggest
189 that sleep problems are an independent predictor of later anxiety, over and above early
190 emotional/behavioural problems (Gregory & O'Connor, 2002), and are more predictive of
191 anxiety/depression than of other psychiatric problems (Johnson, Chilcoat, & Breslau, 2000). Specifically,
192 children who are reported to sleep less than others, and who show overtiredness and have trouble
193 sleeping, have been found to be more likely to score highly on anxiety and depression 14 years later,
194 after controlling for sex, age and anxiety/depression at earlier assessment points (Gregory, Van der
195 Ende, Willis, & Verhulst, 2008). Finally, we were also interested to explore whether associations between
196 responses to emotional faces and 2 year child problems were mediated or moderated by maternal
197 group; i.e. to establish whether responses to emotional expressions explained any association between
198 maternal anxiety status and child symptoms at two years; and/or whether responses to emotional
199 expressions were a better predictor of child anxiety symptoms when they occurred in the context of
200 maternal anxiety disorder.

Method

Sample

203 Mothers attending routine 20-week antenatal clinics completed screening questionnaires to detect
204 possible social phobia and generalised anxiety disorder (GAD). High scoring women were interviewed to
205 confirm diagnosis using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-1; First,
206 Spitzer, Gibbon, & Williams, 1995), administered by trained clinicians. Those meeting criteria for a DSM-
207 IV diagnosis of social phobia or GAD were recruited. Controls were selected randomly from the low-

208 scoring women, who were also interviewed to confirm the absence of psychiatric disorder. A total of 96
209 women were recruited into the social phobia group, 56 were recruited in to the GAD group, and 94 as
210 controls (see Murray, Cooper, Creswell, Schofield, & Sack, 2007, for full recruitment details). Due to
211 tiredness or discomfort not all infants were able to complete the current task. Numbers providing data
212 within the present study were 47 in the social phobia group, 43 in the GAD group, and 60 in the control
213 group. The rate of loss for these reasons (61%) is similar to that reported in other studies of infant
214 looking times (e.g. 53%; Pascalis, de Schonen, Morton, Deruelle, & Fabre-Grenet, 1995); and the fact
215 that it is somewhat higher is likely to reflect the relatively long duration of the current task.

Procedure

Responses to Emotional Expressions.

218 Infants were assessed in university rooms at 10 weeks of age. Infants sat on the experimenter's lap (E1),
219 facing a grey translucent screen within a curtained-booth with low-lighting. The mother and a second
220 experimenter (E2) sat on the other side of the curtains, out of the infant's view. Stimuli (60cm × 76 cm)
221 were displayed in pairs about 5 cm apart on a grey background to match the colour of the projection
222 screen, which was 90 cm distance from the infant. Stimuli were projected from behind the screen using a
223 Sony projector.
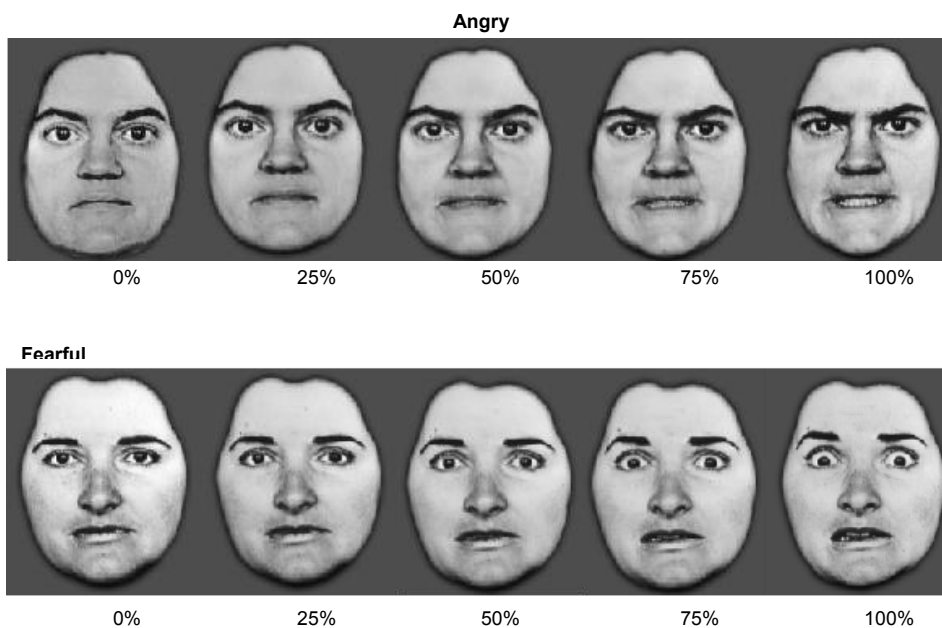
Figure 1: Emotional faces of varying intensity

226 Infant attention was first attracted to the screen by an image of a mobile doll. When the infant fixated on
227 the 'attractor', experimenter E1 pressed a button to notify E2 to start the first trial. Each stimulus pair was
228 presented for 10 seconds. Trials were continued until all stimulus pairs had been presented unless the
229 baby became fractious or fell asleep, in which case the trial was ended prematurely (and data from that
230 set of emotional expressions was not included in analyses). An infra-red video camera was mounted
231 above the projection screen to film the infants' responses. A second camera was mounted behind the
232 screen and recorded the projected images, for verification purposes.

233   To assess infant responses to varying intensities of emotional expression, continua depicting different
234   intensities of anger and fear were taken from the Facial Expressions of Emotion: Stimuli and Tests
235   (FEEST; Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002). Each continuum consisted of a
236   prototype expression face (considered to be 100% intensity for that expression) from the Ekman and
237   Friesen (1976) series, and morphed images interpolated between the prototype expression and its
238   corresponding neutral. So, for example, the neutral face in the Ekman and Friesen series was taken to
239   represent 0% anger, and then 25%, 50%, and 75% angry morphs were created by interpolating between
240   the neutral (0% angry) and the prototype angry (100%) expressions. A different female model was used
241   for each continuum; the stimuli are shown in Figure 1. The faces from the Ekman and Friesen (1976)
242   series used to create these continua were as follows: anger (neutral NR-1-03, anger NR-2-07), fear
243   (neutral MO-1-05, fear MO-1-23). Hairstyles and picture backgrounds were masked, so that all
244   differences between stimuli were only emotion-relevant.

245   Twenty-four face pairs were shown. Within each, one face was shown at 50% intensity and the other
246   showed varying intensities of the same emotion, either anger or fear (8 pairs including each emotion
247   type; 8 pairs of happy faces were also presented but are not considered here). In this way, the standard
248   (50%) face could be of higher or lower emotional intensity than the comparison face. The order of
249   emotion type was counterbalanced across participants and visits. Each face pair was presented for 10
250   seconds, and the same attractor was shown at the start of each trial. The duration of infant looking to
251   each stimulus type within each trial was recorded (i.e. scorers measured duration of looks to the right
252   face, left face, or neither face, using a button box) by scorers who observed infant behaviours on video-
253   tape and were trained to a high level of reliability on a sample of 36 videotapes (ICC = .97). From these
254   data we extracted overall looking times to the different stimuli within each trial, which stimuli the infant
255   looked to first, the length of the first look and the number of looks to each stimulus.

Measures

Adjustment at 2 years of age.

Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000)

259   The CBCL for ages 1 ½ to 5 years was completed by mothers when their offspring were 24 months of
260   age. The CBCL is a widely used instrument composed of 100 items used to assess social and emotional
261   adjustment in youth. The reliability and validity of this measure has been established (e.g. Achenbach,
262   1991). We examined the following subscales: withdrawn, DSM anxiety problems, and sleep problems.   **Comment [CE3]:** Not in ref list
263   The 'withdrawn' scale consists of 8 items (e.g. 'withdrawn, doesn't get involved with others' and 'avoids
264   eye contact'). The DSM anxiety problems scale consists of 10 items (e.g. 'Too fearful or anxious' and
265   'Nervous, 'high-strung', or tense'). The sleep problems scale consists of 7 items (e.g. 'trouble getting to   **Comment [CE4]:** Or highly strung?
266   sleep' and 'wakes up often at night') and is commonly used in sleep research (e.g. Stoleru, Nottelmann,
267   Belmont, & Ronsaville, 1997; Gregory & O'Connor, 2002). Analyses were based on CBCL t-scores.

Data analysis

269   As is standard in infancy research (e.g. Pascalis et al., 2005), cases were excluded from analyses if the
270   infant showed a lateral bias (i.e. they looked to one side (left or right) only throughout all trials for a
271   particular emotion type (Angry faces: Social phobia - 2 cases, GAD – 2 cases, Control – 5 cases; Fear
272   faces: Social phobia - 2 cases; GAD – 3 cases, Control – 3 cases)). Associations between infant
273   responses and gender were first explored; none were significant, so gender was not considered further.
274   In previous studies the side of stimulus presentation has been found to be important, with responses to
275   emotional faces presented on the right side being more pronounced (e.g. Mogg & Bradley, 1999; 2002).   **Comment [CE5]:** Not in ref list- unless you mean 1998?

276 In accordance with this, we found that responses to the left and right side typically did not correlate
277 sufficiently highly to combine them (r = .06 to .73); therefore responses to target faces presented on the
278 right and left were analysed separately. Participants were included if they provided data for all 8 trials
279 within a particular emotion type, i.e. oriented to the attractor at the outset of each trial and remained
280 sitting in front of the stimuli (even if looking away) until the final stimulus was presented. Looking
281 responses to high and low intensity faces conformed to assumptions of parametric tests so comparisons
282 between the pure social phobia and control groups were conducted using repeated measures analysis of
283 variance with proportionate looking times to high and low intensity faces (i.e. time spent looking at the
284 high intensity face vs. the 50% comparator; or time spent looking at the low intensity face vs. the 50%
285 comparator)as the within and group as the between subjects factor. We then repeated these analyses,
286 including the GAD group, with repeated measures ANOVA to address issues of specificity. Where
287 significant group differences were found we, first, assessed the pattern of looking responses in more
288 detail to explore whether differences were consistent with the hypervigilance-avoidance hypothesis using
289 repeated measures analysis of variance for continuous looking responses (i.e. length of first look and
290 number of looks) with looking response as the within-subjects factor and group as the between subjects
291 factor, and chi-square test to examine associations between group and categorical looking responses
292 (i.e. where the infant looked first).

293 Second, we assessed the association between looking responses and outcomes at two years. As
294 outcome data were skewed and were not amenable to transformation, data were dichotomised, using a
295 median split (as this represented a clear cut off point in the data), and binary logistic regression was
296 used to investigate the main effects of group and looking times, and their interaction, in predicting 2 year
297 outcomes. Participant numbers across trials varied due to fatigue/distress or side bias, and therefore
298 separate analyses were conducted to avoid significant data loss.

Results

300 For between group comparisons, effect sizes have been reported as Pearson's correlation coefficient r.

301 *Table 1: Sample characteristics*

	SP (n = 47)	Control (n = 60)	GAD (n = 43)	Statistic
Child sex (% (n) male))	36 (17)	45 (27)	49 (21)	$\chi^2(2)$ = 1.65, p = .44
Maternal age at child birth (mean years(sd))	31.14 (4.03)	31.52 (4.35)	31.25 (3.55)	$F(2,145)$ = .13, p = .88
Marital status (% (n) married and cohabiting)	98 (46)	100 (60)	95 (41)	$\chi^2(2)$ = 2.77, p = .25
Socio-economic status (%(n) professional/ managerial)	70 (33)	72 (43)	74 (32)	$\chi^2(2)$ = .43, p = .81
Ethnicity (%(n) White)	97 (58)	100 (47)	86 (37)	$\chi^2(2)$ = 9.45, p = .01

302 As shown in Table 1, the three study groups were similar in terms of infant sex, maternal age,
303 socioeconomic status and marital status, and the distribution of infant gender. The groups did differ on a
304 broad index of ethnicity, reflecting a larger number of non-white families amongst the GAD group.
305 Nonetheless this reflected a relatively small number of non-white families in the GAD group (n = 6).

306 1. Replication of previous findings with a pure social phobia group

307 Initial analyses included only the social phobia and non-anxious control groups, in order to directly
308 replicate the analyses conducted in our previous paper (Creswell et al., 2008), but restricting the sample
309 to only include offspring of mothers with *pure* social phobia (i.e. not comorbid with GAD as in our

310 previous paper). Responses to emotional expressions were first assessed based on the proportion of
311 time spent looking at the target vs. the 50% expression. No group differences were found in the
312 proportion of time spent looking at the target expression for fearful or angry faces, presented to either
313 side (See Table 2). As we were particularly interested in infants' differential responses to varying
314 intensity emotions, repeated measures analyses were conducted to compare responses to 50%
315 morphed expressions with those to high (75% and 100%) versus low intensity (0% and 25%)
316 expressions.

317 *Table 2: Summed proportions of infant looking time to target versus 50% emotional expressions; Means (sds)*

| Target side	SP (*n* = 45)	Control (*n* = 57)	GAD (*n* = 41)
Angry			
Low (0 & 25%)			
Right	.71 (.50)	.83 (.59)	.86 (.55)
Left	1.17 (.61)	1.16 (.59)	1.00 (.57)
High (75 & 100%)			
Right	.97 (.62)	.72 (.49)	1.01 (.57)
Left	1.23 (.66)	.83 (.59)	1.17 (.57)
Fearful			
Low (0 & 25%)			
Right	1.08 (.68)	.98 (.66)	.92 (.56)
Left	1.14 (.73)	1.02 (.60)	1.11 (.52)
High (75 & 100%)			
Right	.85 (.58)	1.00 (.61)	.87 (.56)
Left	1.11 (.61)	1.10 (.59)	1.03 (.58)
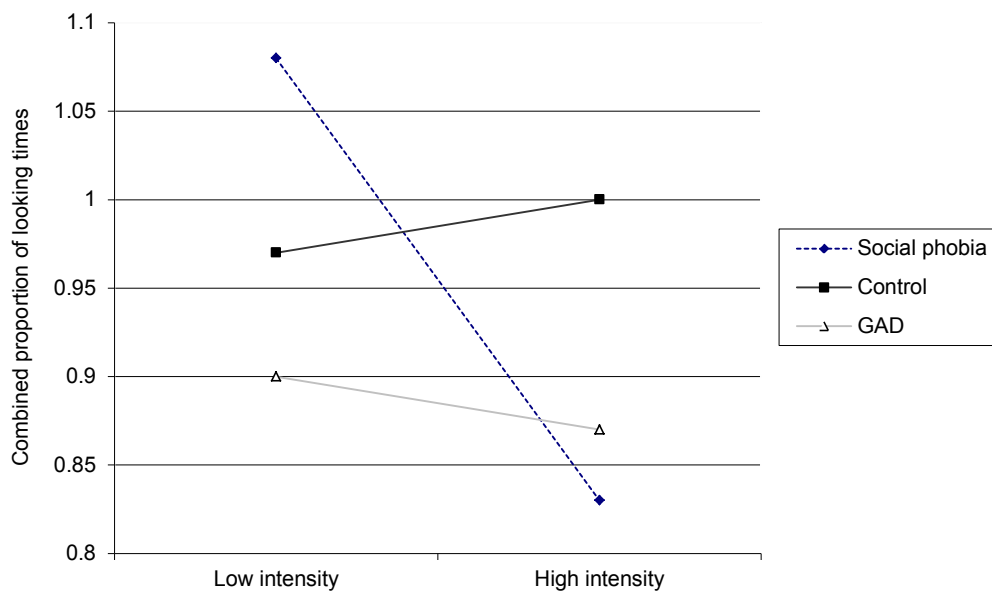
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319 *Figure 2: Interaction between participant group and level of emotional intensity of fearful expressions (presented on*
320 *the right side)*

321 For fearful faces, the between subjects effect of group was not significant; however, the within subjects
322 effect of intensity approached significance when the target stimulus was presented on the right, $F(1, 62)$
323 = 3.11, p = .08, r = .22 and there was a significant interaction effect of intensity × group, $F(1, 62)$ = 4.51,
324 p = .04, r = .26, see Figure 2. Post-hoc analyses confirmed a pattern of reduced looking to high vs. low
325 intensity fearful faces among infants of mothers with social phobia, $t(27)$ = 2.88, p = .01, but not control
326 infants, $t(35)$ = .25, p = .80. This reflected a greater *difference* in looking to high vs. low fear faces in the
327 social phobia group (looking to high-low fear faces: SP *mean* = 0.26 (.47), control mean = 0.02 (.56),
328 $t(52)$ = 2.12, p = .04). Neither the main effect of intensity, $F(1, 57)$ = .14, p = .62, nor the interaction with
329 group, $F(1, 57)$ = .31, p = .58 were significant when the target stimulus was presented on the left,
330 although the pattern of results was the same.

331 For angry faces, there was no significant between subjects effect of group or within subjects effect of
332 intensity when the target stimulus was presented on either side; however, there was a significant
333 interaction between intensity and group (SP vs. control) when the target was presented on the right, $F(1,$
334 76) = 4.77, p = .03; r = .24, see Figure 3, reflecting a pattern of significantly increased looking to high vs.
335 low intensity faces amongst the offspring of mothers with social phobia, $t(31)$ = 2.35, p = .02, and a non-
336 significant reduction in looking to high vs. low intensity angry faces among offspring of control mothers,
337 $t(45)$ = .52, p = .60). As with fearful faces, this reflected a greater difference in looking times amongst
338 infants of mothers with social phobia, but this time in the reverse direction to the pattern with fear faces
339 (looking to high-low angry faces: SP mean = 0.23 (.23), control mean = −0.04 (.53), $t(76)$ = 2.18, p =.
340 03). This interaction was not significant when the target was presented on the left, $F(1, 76)$ = 2.55, p =
341 .12, r = .18), although the pattern of results was the same.
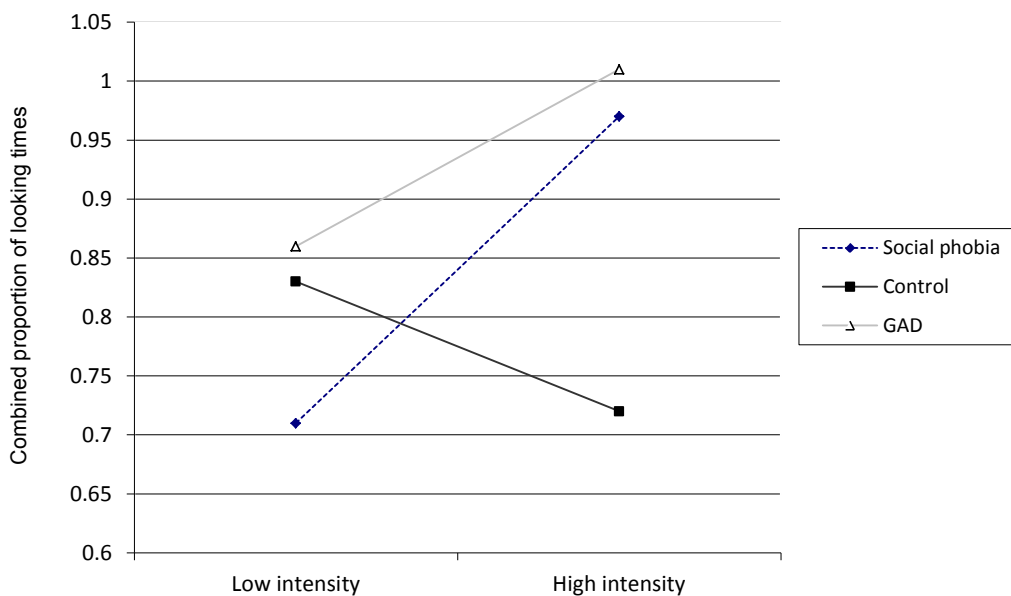
342

343 *Figure 3: Interaction between participant group and level of emotional intensity of angry expressions (presented on*
344 *the right side)*

345 In order to address patterns of looking in greater detail (specifically to ascertain whether findings were
346 consistent with initial hypervigilance/ avoidance), we compared infant responses to high intensity angry

347   and fearful faces presented on the right, on the following: (i) which stimulus the infant looked to first
348   (target/control), (ii) the length of the first look to target/control stimuli; and (iii) the total number of looks to
349   target/control stimuli. For fearful faces, there was no significant difference between groups on where the
350   infant looked first, $\chi^2(1) = 51$, $p = .48$, or interactions between group and either the length of the first look
351   to the target versus control stimuli, $F(1, 75) = .82$, $p = .37$), or the number of looks to target vs. control
352   stimulus, $F(1, 74) = .03$, $p = .86$). For angry faces, there was a significant difference between infants of
353   mothers with social phobia and control mothers in terms of where they looked first when presented with
354   a high intensity face as part of the face pair, with infants of mothers with social phobia being less likely to
355   look to the high intensity face first (64% vs. 94%; $\chi^2(1) = 9.25$, $p < .01$). There were no significant
356   interactions, however, between maternal group and either the length of the first look to the high intensity
357   target versus control stimuli, $F(1, 65) = .01$, $p = .91$), or the number of looks to high intensity target vs.
358   control stimulus, $F(1, 65) = .01$, $p = .91$).

359   2. Specificity of the findings in comparison to infants of mothers with GAD

360   Next, we were interested to determine to what extent the infant responses to emotional faces that
361   discriminated infants in the social phobia and control groups, were specific to offspring of mothers with
362   social phobia in comparison to offspring of GAD mothers. As above, the variables of interest were (i) the
363   difference in looking time proportions to high and low intensity faces (proportion of time looking to high
364   intensity - proportion of time looking to low intensity faces), and (ii) location of first looks (target vs.
365   control); and for fearful faces (iii) the difference in looking time proportions to high and low intensity faces
366   (proportion of time looking to high intensity - proportion of time looking to low intensity faces); all of which
367   when presented on the right side.

368   When all three groups were considered, the main effects of intensity, the group and the group-intensity
369   interaction were no longer significant for fear faces, however, the pattern of results suggest that the GAD
370   group showed a less marked reduction in looking to high intensity fear faces than the social phobia
371   group, and they appear to more closely resemble the pattern of the control group (see Figure 2).

372   For angry faces, the between subjects effect of group was not significant, $F(2, 115) = 1.91$, $p = .15$, but
373   there was a significant effect of intensity, representing higher overall looking times to high intensity angry
374   faces, $F(1, 115) = 4.65$, $p = .03$, $r = .20$). The group $\times$ intensity interaction approached significance, $F(2,$
375   $115) = 2.49$, $p = .09$, $r = .13$, however this appeared to reflect the significant interaction when the social
376   phobia and control groups were considered, as the interaction was not significant when analysed with
377   either the social phobia, $F(1,70) = .41$, $p = .53$, or the control groups, $F(1,84) = 2.38$, $p = .13$, $r = .17$. As
378   shown in Figure 3, both infants of mothers with GAD and those of mothers with social phobia showed
379   increased looking to high intensity angry faces, whereas infants of control mothers looked slightly less to
380   high intensity than low intensity faces. Post-hoc analyses confirmed that the interaction was significant
381   when only the social phobia and control groups were included, but not with the social phobia and GAD
382   groups, $F(1, 70) = .41$, $p = .53$, or the GAD and control groups, $F(1, 84) = 2.38$, $p = .13$, $r = .17$. As
383   shown in Figure 3, the group difference appeared to be most marked for high intensity angry faces;
384   therefore, follow-up analyses were conducted to explore this further. There was a significant group effect
385   for the proportion of time spent looking at the high intensity angry faces presented on the right, $F(2, 118)$
386   $= 3.41$, $p = .04$, $r = .17$. Post-hoc t-tests confirmed that this reflected increased looking to high intensity
387   angry faces by both the social phobia group, $t(79) = 2.05$, $p = .04$, $r = .22$ and GAD group, $t(84) = 2.51$, p
388   $= .01$, $r = .26$, in comparison to the control group, and no significance difference between the social
389   phobia and GAD groups, $t(73) = .26$, $p =. 80$.

390   A significant difference was found for the location of the first look compared across groups, $\chi^2(2) = 9.49$,
391   $p = .01$. This represented an increased rate of looking first to the high intensity angry face (vs. the

392 control) for infants of non-anxious (94%) followed by GAD (83%) and finally socially phobic (64%)
393 mothers. Post-hoc analyses showed that this represented significant difference between the social
394 phobia and control groups (χ^2(1) = 9.25, p < .01), and a trend difference between the GAD and social
395 phobia groups, χ^2(1) = 2.97, p =.09, but no significant difference between the GAD and control groups
396 χ^2(1) = 2.25, p = .13.

397 3. Associations with outcomes at 2 years

398 To explore associations between looking responses to emotional faces at 10 weeks and outcomes at 2
399 years, we focused on those variables that had been identified as distinguishing between infant groups,
400 i.e. for fearful faces, (i) the difference between looking times to high and low intensity faces; and for
401 angry faces, (ii) the difference between looking times to high and low intensity faces, (iii) looking times to
402 high intensity faces, and (iv) location of first looks (target vs. control) when presented on the right side.
403 As few children scored above borderline/clinical cut-offs (i.e. anxiety problems 4.3%; withdrawn 1.2 %;
404 sleep problems 4.3%), CBCL variable scores were dichotomised on the basis of frequency distributions
405 (which led to data being split at the median in all cases).

406 Logistic regression analyses were conducted, with dichotomised CBCL scores as the dependent
407 variables, and group, looking response (i.e. the four looking response variables outlined above) and their
408 interaction as the predictor variables. For CBCL anxiety problems, none of the main effects of group or
409 looking responses were significant, however, there was a significant effect of the interaction between
410 (social phobia) group and difference in looking time to high and low intensity fear faces, $exp(B)$ = 14.28,
411 p = .04, see Table 3. To probe the interaction, the binary logistic regression was run to examine the
412 effects of group when the difference in looking to high and low intensity fear faces was set (at the mean
413 plus one standard deviation above and one standard deviation below the mean). This confirmed a
414 significant effect of social phobia group when the difference score was high, $exp(B)$ = 7.39, p = .05. The
415 effect of GAD group when the difference score was high approached significance, $exp(B)$ = 4.68, p = .06.
416 Group effects were not significant when the difference score was low.

417 *Table 3: Prediction of CBCL anxiety problems at two years from maternal group and high- low looking to fear faces*

		95% CI for Odds Ratio		
	B (*SE*)	Lower	Odds ratio	Upper
Included				
Maternal group (SP vs. others)	.69 (.63)	.58	1.19	6.90
Maternal group (GAD vs. others)	.62 (.58)	.60	1.16	5.75
Looking to high fear/ Looking to low fear	0.92 (.76)	.09	1.46	1.77
Group (SP) x Looking response	2.66 (1.34)*	1.03	3.93	197.64
Group (GAD) x Looking response	-.57 (.40)†	.87	2.01	48.65

418 R^2 = .09 (Cox a& Snell), R^2 = .12 (Nagelkerke), Model χ^2(5) = 7.48, p = .19

419 As looking responses did not have an independent effect on CBCL anxiety problems, mediation
420 hypotheses were not pursued further. There were no significant main effects or interactions in relation to
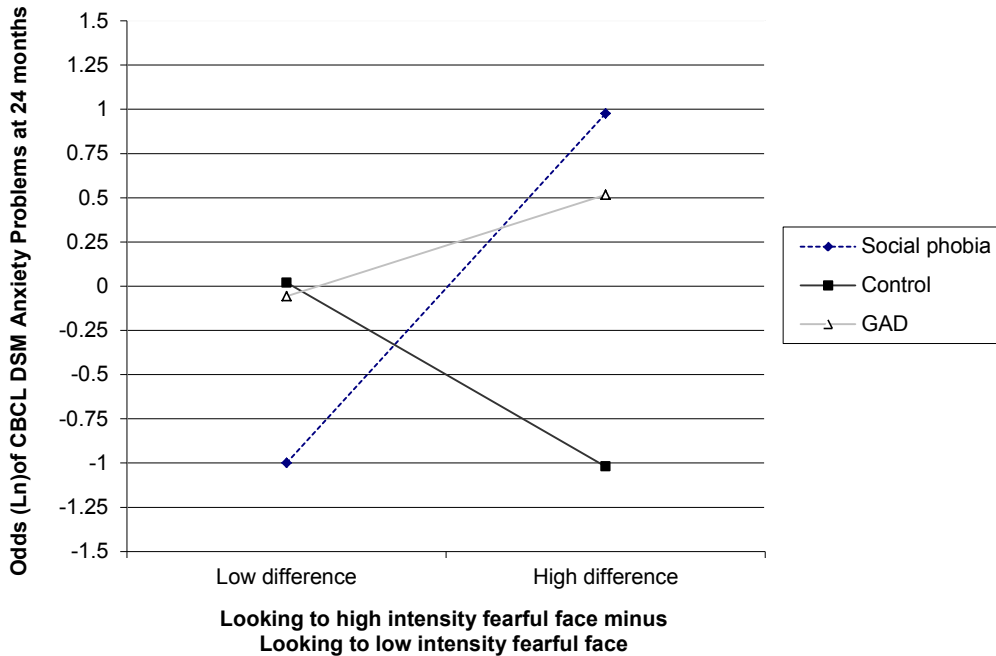421 sleep or withdrawn problems.

Figure 4: Prediction of CBCL anxiety at two years from maternal group and difference between high and low looking to fear faces

Discussion

Socially anxious adults and children show biases in their looking responses to emotional faces (e.g. Bögels & Mansell, 2004; Garner, 2010), and consistent patterns have been found among infants at hereditary risk of social phobia (Creswell et al., 2008). This study set out to evaluate whether these patterns are specific to infants at risk of social phobia, in comparison to infants at more general risk of anxiety problems (i.e. infants of mothers with GAD), and to identify whether early responses to emotional expressions are associated with emerging anxiety symptoms assessed at two years of age.

As the current study limited the index group of participants to infants of mothers with *pure* social phobia (i.e. not those with comorbid GAD), we first set out to establish whether the findings from our previous report were maintained with this restricted group (Creswell et al., 2008). The results were partially replicated. As before, there were no group differences in overall looking times to particular stimuli, however groups did differ in their relative looking to high and low intensity stimuli (each presented alongside a 50% intensity expression), when target stimuli were presented on the right side. As before, we found a significant interaction between maternal group and emotional intensity for fear faces, reflecting less relative looking time to high intensity faces among infants of mothers with social phobia compared to non-anxious mothers. In other words, infants of socially phobic mothers preferred the 50% control expression to the high intensity stimulus, but preferred the low intensity face to the 50% control expression; thus, infants of mothers with social phobia showed a preference in all cases for the lower intensity fear expression of the pair. For infants of control mothers, however, there was no significant evidence for a preference. In our previous report we noted that, for fearful faces, infants of socially phobic mothers looked less frequently to the target stimulus first, however, this was not significant with

446 this smaller group of infants of mothers with pure social phobia. The effect size was substantially lower
447 than in our previous report, which suggests that the effect may have been substantially influenced by the
448 inclusion of comorbid cases previously, rather than the difference arising as a function of sample size.

449 In our previous paper we did not find any significant results in relation to angry faces; however, with the
450 current pure social phobia group, we did find a significant interaction between group and emotional
451 intensity (again when the target as presented on the right side). For angry faces, we saw the reverse
452 pattern from fear faces, i.e. infants of socially phobic mothers looked relatively more to high intensity
453 faces, whereas infants of non-anxious mothers looked relatively more to low intensity faces. In other
454 words, infants of socially phobic mothers showed a preference for the higher intensity face in each face
455 pair (when presented with a high intensity face next to a 50% face they would show more looking to the
456 high intensity face, and when presented with a low intensity face next to a 50% face they would show
457 more looking to the 50% face). The infants of the non-anxious mothers showed the reverse pattern. In
458 terms of initial looking, the index infants were more likely to look first to the 50% expression than the
459 control group, but there were no differences in the length of the first look or number of looks overall to
460 each stimulus. Overall, the findings for neither fear nor angry faces are consistent with a pattern of
461 hypervigilance-avoidance for threat, however, overall, infants of mothers with social phobia appear to
462 attend preferentially *away* from higher intensity fear faces, and *towards* higher intensity angry faces.

463 When infants of mothers with GAD were also considered, the interaction between group and emotional
464 intensity for fear faces was no longer significant, which most probably reflected the loss of power from
465 the inclusion of a third group. For angry faces, however, the social phobia and GAD groups displayed a
466 similar pattern of responding, in which both looked more to high intensity angry faces, in comparison to
467 the control infants. When high intensity faces were presented alongside the 50% control, infants of non-
468 anxious mothers were significantly more likely to look to the target first in comparison to the social
469 phobia and GAD groups, suggesting that the increased overall looking to high intensity faces seen
470 amongst the anxiety groups was not based on early hypervigilance to the high intensity face.

471 The pattern of results is consistent with the conclusion that risk for social anxiety may be associated with
472 avoidance of fearful faces; whereas risk for anxiety generally is associated with a vigilance towards
473 angry faces. This conclusion is consistent with previous findings in a community population that indicated
474 that social anxiety symptoms are associated with reduced attention to fearful faces (Stirling et al., 2006),
475 and findings from clinical populations that children with GAD show attention towards angry faces (Monk
476 et al., 2008; Waters et al., 2008). The results are contrary, however, to findings that *reduced* attention to
477 angry faces was associated with levels of social anxiety in community participants (Stirling et al., 2006)
478 and also the presence of a GAD diagnosis (Monk et al., 2006). While our results require replication, it
479 does seem plausible that, in infants, anger and fear presentations may evoke different response
480 patterns, as these expressions serve clearly different functions, with angry faces reflecting a threat, and
481 fear faces reflecting a warning sign. According to this interpretation, our results would suggest that a
482 hereditary risk for anxiety is associated with a bias towards threat information; but a hereditary risk for
483 social anxiety specifically is associated with a bias away from warning signs.

484 In terms of associations with children's anxiety-related symptoms at two years of age, we considered
485 symptoms of social-withdrawal, general anxiety, and also sleep problems. Findings were strongest in
486 relation to general anxiety problems. Specifically, risk for problems was increased if infants of mothers
487 with social phobia displayed higher relative looking times to high (vs. low) intensity fear faces at 10
488 weeks. In other words, when infants of socially anxious mothers showed a preference for low intensity
489 fear faces this was associated with a better outcome at two years, than when they showed a preference
490 for high intensity fear faces. We did not find any significant main or interaction effects in relation to sleep

491 problems at two years. Whilst conclusions must remain tentative, this may reflect these particular
492 problems being more a response to environmental factors (e.g. care practices) than endogenous factors.

493 The interactive effects of infant looking response and maternal group are intriguing. While infants of
494 mothers with social phobia are more likely to show reduced looking to fearful faces, those that do not
495 show this pattern appear to be at increased risk of anxiety symptoms at two years of age. Any
496 conclusions must remain tentative and the results require replication, however one possible explanation
497 is that a tendency for infants to prefer fear faces may elicit particular responses from anxious (but not
498 non-anxious) mothers. For example, anxious mothers may respond to infant interest in fear faces, and
499 related stimuli, with reduced levels of social encouragement, which may lead to increases in infant
500 anxiety as the child develops social understanding through social referencing processes in the period
501 between our two assessment points (e.g. Murray et al., 2008). Future studies would benefit from the
502 inclusion of measures to test and power to test these transactional processes.

503 It is important to note that, for infant responses to emotional expressions, the side of presentation of the
504 index face was important and the interaction effects of group and intensity of fearful and angry
505 expressions were most pronounced for presentations on the right. Our results are consistent with those
506 of other studies with adults (Mogg & Bradley, 1999, 2002), suggesting that lateralised brain mechanisms
507 may play a critical role in the processing of face stimuli (Morris, Ohman, & Dolan, 1998). Conclusions
508 with regards the specificity of findings to stimuli presented on the right must, however, remain tentative.

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509 There are various reasons to consider our results with caution. In particular, significant results reflect
510 modest effects sizes and, as such, maternal group appears to explain a relatively small proportion of the
511 variance in children's responses to emotional expressions. Due to the novelty of the approach, we did
512 not want to be overly conservative in an attempt to reduce Type 1 error, however, it must be
513 acknowledged that a relatively large number of univariate tests were conducted. As young infants can be
514 expected to frequently become fatigued or unsettled, the number of trials that we administered was low
515 (e.g. two high intensity faces of each emotion type on each side of presentation). Even so, there were a
516 substantial number of infants with incomplete trials, which limited the use of multivariate analyses and
517 restricted the power of the study, which may have led to Type 2 error. Second, our assessment of child
518 adjustment was based on maternal report. While the CBCL is a widely used measure with established
519 reliability, maternal reports may be influenced by levels of maternal anxiety (Briggs-Gowan, Carter, &
520 Schwab-Stoar, 1996). In addition, it is important to note that while differences were found in relation to
521 CBCL outcomes, very few children scored within the borderline or abnormal ranges, and as such
522 differences reflected relatively small differences in nonclinical symptom levels. Finally, the current study
523 is not able to differentiate between different classes of risk, such as genetic risk, effects of antenatal
524 anxiety and stress (e.g. O'Connor, Heron, Golding, & Glover, 2003; ven den Bergh & Marcoen, 2004) or
525 antenatal medication.

526 With these limitations in mind, the current study provides further support for the integral bias hypothesis,
527 in that evidence for biases in responses to emotional expressions was evident in young infants at
528 hereditary risk of anxiety and social phobia (e.g. Richards et al., 2002). Whereas attention towards angry
529 faces is associated with a general risk for anxiety, attention away from high intensity fear faces is
530 associated with a more specific risk for social anxiety. Infants of anxious mothers who fail to show this
531 early pattern, however, appear to be at increased risk of anxiety symptoms at two years. Aside from the
532 need for replication, future studies would benefit from longitudinal assessments of continuity and change
533 in responses to emotional expressions in order to track their associations with anxiety symptoms in later
534 childhood and adolescence.

Comment [CE8]: Not in ref list

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