Adolescents’ depressive symptoms moderate neural responses to their mothers’ positive behavior

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The way that parents express their emotions during interactions with their adolescent children is important for adolescent adjustment, and predicts adolescent emotional problems such as depression. In the current study, we assessed whether adolescent depressive symptoms were associated with neural activity during exposure to one’s own or an unfamiliar mother’s positive behavior. Thirty adolescents (18 females, mean age 17.35, s.d. 0.43) participated in an fMRI task that used digitized video segments of their own mother’s affective behavior as stimuli. Exposure to one’s own (compared to an unfamiliar) mother’s positive behavior was associated with activation in the anterior and posterior cingulate, precuneus and ventrolateral prefrontal cortex. In contrast, exposure to positive behavior by one’s own (compared to an unfamiliar) mother’s positive behavior, and reduced striatal activity during exposure to positive behavior in adolescents. Further, the results support a disruption of reward function in depression.

Keywords: family; depression; adolescence; anterior cingulate cortex; emotion

INTRODUCTION

Adolescence marks a period of increased risk for major depressive disorder (MDD) (Lewinsohn et al., 1993, 1998). This increased risk is thought to be associated with a failure to adapt to the myriad of biological and environmental changes occurring during this time (Arnett, 1999), which in turn leads to problems with emotional responding and regulation for some adolescents (Kovacs and Lopez-Duran, 2010). One environmental change that has been identified as important in adolescent emotional adjustment and depression is the renegotiation of roles in the family home as adolescents become more independent (Brooksgunn and Petersen, 1991). Indeed, family relationships appear to be stronger predictors of adolescent depression than peer relationships (Stice et al., 2004), and the way adolescents react to and regulate their emotions during interactions with their parents has been found to be associated with adolescent depressive symptoms (Davis et al., 2000; Yap et al., 2010). Thus, abnormal adolescent affective experience in the context of the parent–child relationship might be particularly important for the development of depression in adolescence.

Relative to adult studies, there are currently few brain imaging studies that have investigated neural function associated with affective processing in adolescent depression. These studies show adolescent depression to be associated with altered reward-related responding in the striatum, medial prefrontal cortex (PFC), orbitofrontal cortex and amygdala (Forbes et al., 2006, 2010), and with altered responding in the ventromedial PFC, anterior cingulate cortex (ACC) and amygdala in response to negative affective stimuli (Beesdo et al., 2009; Killgore and Yurgelun-Todd, 2006; Thomas et al., 2001). These abnormalities not only appear to show some similarities, but also some differences, to adult findings (Yang et al., 2010), and the small number of studies prevents any conclusive interpretation of findings. Further, the research available has typically used stimuli of low personal salience and low ecological validity (e.g. static images of...
unfamiliar faces, Forbes et al., 2010; Yang et al., 2010). Though these stimuli provide the benefit of standardization, they limit inferences that can be made about emotion processing of meaningful, real-world experiences.

Further, a few studies with healthy adolescents (Guyer et al., 2009; Masten et al., 2009; Davey et al., 2010; Sebastian et al., 2010) and adolescents at risk for depression (Masten et al., 2011) have investigated affective neural responses using more ecologically valid designs (e.g. simulated social rejection). However, the paradigms employed typically involve reference to social situations with unknown individuals, potentially limiting the personal relevance to participants. No adolescent imaging studies to-date have utilized personally relevant stimuli that more realistically approximate the emotional experiences of adolescents in their day-to-day lives, and which might be more relevant to the development of depressive symptoms and disorders. Further, few studies have used dynamic (vs static) stimuli, which is likely to reveal more ecologically valid neural responses (Fine et al., 2009).

There were two main objectives of this study. First, we aimed to investigate the neural basis of adolescent affective experience using stimuli that, compared to traditional paradigms, better approximate the real-world environment, and hence are more likely to invoke the types of emotional responses adolescents experience in their day-to-day lives. To this end, we employed a novel fMRI paradigm that expands upon our previously piloted work (Forbes et al., 2009b) whereby stimuli were dynamic audio-visual recordings of the adolescent’s own mother, which were obtained during emotionally evocative mother–adolescent discussions. We compared adolescents’ brain activity while viewing these video clips to that evoked by viewing comparable video clips of an unfamiliar mother. Second, given that the mother–child relationship (and in particular, the way that adolescents respond to and regulate their emotions during interactions with their mothers) has been suggested as important for the emergence of depression during adolescence, we aimed to investigate whether adolescent depressive symptoms were associated with brain function during exposure to the video-clip stimuli. Recruiting a sample of adolescents with a wide range of depressive symptoms allowed us to investigate brain function associated with the full range of symptoms representative of those in the population. In order to achieve this, participants were selected to encompass a wide range of depressive symptoms (range = 1.67–35, mean = 12.18; s.d. = 9.15) based on average Center for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1977) scores measured at three time-points when adolescents were, on average, 12.51 (s.d. 0.39), 15.03 (s.d. 0.46) and 16.60 (s.d. 0.32) years of age. As noted below, this selection procedure resulted in a sample of participants with a wide range of current (i.e. measured on the day of the MRI scan) depressive symptoms (CES-D score range 1–29). Further, current depressive symptoms were significantly correlated with past average depressive symptoms (r = 0.68, P < 0.001). Nine participants had a lifetime history of mental illness, established at an assessment conducted within the previous year using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children: Epidemiologic Version (Kaufman et al., 1997): MDD = 5 (two with comorbid simple phobia, one with comorbid social phobia, one with comorbid conduct disorder and cannabis dependence), adjustment disorder with depressed mood = 1, social phobia = 2 (one with comorbid generalized anxiety disorder), oppositional defiant disorder = 1. Based on a cut-off score of >28 (Yang et al., 2004) on the CES-D (completed post-scan, see below), one participant met criteria for clinically significant depressive symptoms at the time of assessment. No participants were taking psychoactive drugs at the

methods and materials
Participants
Participants were 30 (18 females) adolescents (mean age 17.35 years, s.d. 0.43 years) recruited as part of a broader longitudinal study designed to examine risk for depression (The Orygen Adolescent Development Study, see Whittle et al., 2008 for further details). As mentioned above, we recruited a sample of adolescents with a wide range of depressive symptoms so that we could investigate brain function associated with the full range of symptoms representative of those in the population. In order to achieve this, participants were selected to encompass a wide range of depressive symptoms (range = 1.67–35, mean = 12.18; s.d. = 9.15) based on average Center for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1977) scores measured at three time-points when adolescents were, on average, 12.51 (s.d. 0.39), 15.03 (s.d. 0.46) and 16.60 (s.d. 0.32) years of age. As noted below, this selection procedure resulted in a sample of participants with a wide range of current (i.e. measured on the day of the MRI scan) depressive symptoms (CES-D score range 1–29). Further, current depressive symptoms were significantly correlated with past average depressive symptoms (r = 0.68, P < 0.001). Nine participants had a lifetime history of mental illness, established at an assessment conducted within the previous year using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children: Epidemiologic Version (Kaufman et al., 1997): MDD = 5 (two with comorbid simple phobia, one with comorbid social phobia, one with comorbid conduct disorder and cannabis dependence), adjustment disorder with depressed mood = 1, social phobia = 2 (one with comorbid generalized anxiety disorder), oppositional defiant disorder = 1. Based on a cut-off score of >28 (Yang et al., 2004) on the CES-D (completed post-scan, see below), one participant met criteria for clinically significant depressive symptoms at the time of assessment. No participants were taking psychoactive drugs at the
Depression, fMRI and real-world stimuli

Measures

In order to obtain current depressive symptoms, participants completed the CES-D post-scan, which assesses depressive symptoms over a 2-week period. In addition, participants viewed the video-clip stimuli outside the scanner and rated their own happy, sad, anxious and angry affective responses, as well as perceptions of their own/other mother’s affect, during each clip using visual analog scales (range 0–100). The purpose of this was to validate the externally coded video clips, and to allow examination of whether these ratings moderated any of the neuroimaging findings.

Magnetic resonance imaging

Whole-brain functional data were acquired on a 3T Siemens MAGNETOM Trio whole-body MRI scanner in 40 contiguous oblique axial slices (3 mm thick, 3 mm² in-plane resolution) with a T2*-weighted echo-planar imaging (EPI) sequence [repetition time (TR) = 2500 ms, echo time (TE) = 30 ms, flip angle = 85°, field of view (FOV) = 216 mm] in two runs of 174 volumes each (435 s). Structural data were acquired with a T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) scan (160 slices, 1 mm² in-plane resolution; TR = 1900 ms, TE = 2.55 ms, flip angle = 9°, FOV = 256 mm).

fMRI stimuli

Stimuli were video segments of the adolescent’s own mother or an unfamiliar mother displaying positive, aggressive or neutral affective behavior. The own-mother clips were recorded ~4.5 years earlier during interaction tasks in which the mother–adolescent dyad engaged in 20 min problem-solving (PSI) and event-planning (EPI) conversations in the laboratory (see Yap et al., 2008 for further details). The unfamiliar mother was an actor trained to simulate the interactions (with an adolescent actor) using conversation topics typical of the own-mother–adolescent interactions. For both own- and unfamiliar-mother clips, footage contained only the mother, framed to include the entire head and upper torso, with a neutral background, and the mother’s gaze directed off-camera towards the adolescent. Video clips contained audio that was predominantly from the mother, without marked stress on individual syllables. For one participant, only 10 s of continuous own-mother positive affective behavior was available (other periods of positive behavior were available but were very short), so this segment was looped to create a 20 s clip. For five participants, 20 s of continuous aggressive (n = 4) or positive (n = 1) mother behavior was not available, so two separate (~10 s) segments containing the behavior of interest were played consecutively. Participants with continuous video footage did not differ from those with looped or concatenated video footage on current depressive symptoms [t(28) = 0.31, P = 0.762].

fMRI paradigm

The 20 s video clips were presented in a block design, interspersed with 15-s rests (fixation cross-hair), during two 7.25-min runs. Within each run, neutral, positive and aggressive clips were alternated within alternating own- and unfamiliar-mother clips (i.e. own-neutral, unfamiliar-positive, own-aggressive, unfamiliar-neutral, etc.). Once all six clips had been presented in this alternating fashion, they were repeated in the same order, such that for each run there were two presentations of each clip. The order of presentation was counterbalanced across runs and participants. Participants were not required to make any responses during the paradigm. This was to maximize our ability to examine naturalistic neural function.

Statistical analysis

Behavioral.

Repeated measures analyses of variance (ANOVAs) were conducted to test for the effects of mother (own and unfamiliar), clip (aggressive, positive and neutral) and emotion (happy,
sad, angry and anxious) on adolescents’ (post-scan) ratings of (i) their own affective response while watching the video clips and (ii) the mother’s affect during the video clips. We also calculated the frequency of mother aggressive behavior (rate per minute) across the entire duration of the 20-min PSI and EPI interactions from which the own-mother clips were derived. These measures have been used in previous studies as an index of family relationship quality (Burgess et al., 1978), and have shown relationships with poorer cognitive and psychosocial outcomes in children (Forgatch, 1989; Eddy et al., 2001), including depression (Yap et al., 2008). These measures allowed us to investigate whether quality of the mother–child relationship moderated neuroimaging findings. We investigated the association between depressive symptoms and (a) post-scan ratings and (b) frequency of mother aggressive behavior during the PSI and EPI using Pearson’s correlations.

**fMRI.**

fMRI data analysis was carried out using FMRI Expert Analysis Tool version 5.98, part of FSL (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistical processing was applied: rigid-body motion correction, removal of non-brain structures, spatial smoothing using a Gaussian kernel of full width at half maximum of 8 mm, and high-pass temporal filtering with a frequency cut-off point of 120 s. Functional images of each participant were co-registered to structural images in native space using FMRIB Linear Image Registration Tool (FLIRT) for linear (affine with six degrees of freedom) registration (Jenkinson and Smith, 2001), and structural images were normalized to structural standard images, defined by the Montreal Neurological Institute (MNI) standard brain supplied in FSL (Avg152, T, 2 × 2 × 2 mm), using FLIRT non-linear transformation (12 degrees of freedom). The same transformation matrices used for structural-to-standard transformations were then used for functional-to-standard space transformations of co-registered functional images. One run for each of three participants was excluded from further analysis due to excessive motion (relative displacement in any direction ≥ 2 mm), however, the other run for these participants were included in analyses.

Individual activation maps for each run were computed using the general linear model. Six explanatory variables were modeled (positive, aggressive and neutral behavior for each of own- and unfamiliar-mother). The contrasts that we were specifically interested in were the main effects of positive and aggressive affect (i.e. positive > neutral and aggressive > neutral, respectively, collapsed across own- and unfamiliar-mother), and the interaction between mother and affect for positive and aggressive affect [e.g. (own-mother positive > own-mother neutral) > (unfamiliar-mother positive > unfamiliar-mother neutral)]. All regressors were modeled by convolving the onset of each stimulus with a canonical hemodynamic response function using a variant of a $\gamma$-function with a standard deviation of 3 s and a mean lag of 6 s.

The two runs for each participant were combined using a fixed-effects statistical framework. Group-level random-effects components of mixed-effects variance were then modeled and estimated using FLAME Stage 1 (Beckmann et al., 2003). Z (Gaussianized T/F) image statistics were calculated with a threshold of $Z=3.1$ at the voxel level and were cluster level corrected to account for multiple comparisons at a significance threshold of $P<0.05$ (Worsley et al., 1992).

We assessed whether adolescent depressive symptoms, frequency of maternal aggressive behavior (PSI and EPI), ratings of their own affect, and perceptions of their mother’s affect were associated with activations for each contrast of interest. Demeaned scores/ratings were entered as covariates of interest in group-level analyses using corrected group activation maps (resulting from the contrasts of interest, described above) to mask the search area prior to thresholding results at $P<0.001$, uncorrected, with a cluster extent threshold of 10 voxels (Forman et al., 1995).

**RESULTS**

**Behavioral**

Mean CES-D score assessed post-scan was 11.4 (s.d. 7.1, range 1–26). Means and standard deviations for the adolescents’ video-clip ratings are given in Table 1. For own affect ratings, ANOVA revealed a significant clip × emotion interaction [$F(6,174) = 22.83, P<0.001$]. As expected, positive video clips were rated highest for happy affect and aggressive video clips were rated highest for angry affect. For mother affect ratings, ANOVA revealed a significant mother × clip × emotion interaction [$F(6,168) = 4.98, P<0.001$] interaction. For both own and unfamiliar mother, positive video clips were rated highest for happy affect and aggressive video clips were rated highest for angry affect, but happy and angry ratings were more pronounced (i.e. of greater magnitude) for the unfamiliar-mother.

Depressive symptoms were positively associated with the frequency of mother aggressive behavior during the EPI ($r=0.434, P=0.017$) and trended towards significance for the PSI ($r=0.330, P=0.075$). Depressive symptoms were also significantly associated with greater reported levels of negative affect during the own-mother (own angry: $r=0.373$, $P=0.042$; own anxious: $r=0.389$, $P=0.034$; mother anxious: $r=0.403$, $P=0.027$) and the other-mother (own sad: $r=0.443$, $P=0.014$; own angry: $r=0.518$, $P=0.003$; own anxious: $r=0.617$, $P<0.001$; mother sad: $r=0.390$, $P=0.033$; mother anxious: $r=0.535$, $P=0.002$) positive clips, but were ‘not’ significantly correlated with any of the adolescent ratings of the own-mother or the other-mother aggressive clips (all $P>0.05$).
fMRI

**Positive behavior**

The main effect of positive affective behavior (i.e. positive > neutral, collapsed across own- and unfamiliar-mother) was associated with extensive bilateral activation in the superior temporal sulcus (STS); this activation extended into the frontal orbital cortex in the left hemisphere (Table 1 and Figure 1). Positive behavior was also associated with activation in the occipital pole, as well as bilateral activation in the amygdala, which in the right hemisphere extended into the hippocampus and pallidum/putamen.

**Aggressive behavior**

The main effect of aggressive behavior (i.e. aggressive > neutral, collapsed across own- and unfamiliar-mother) was associated with extensive bilateral activation in the STS, extending into the temporal poles and frontal orbital cortex (Table 1 and Figure 2). Aggressive behavior was also associated with medial PFC activity that extended into the rostral ACC (rACC), bilateral activity in the thalamus and activity in the left occipital pole extending into the posterior cerebellum.

**Mother-affect interactions**

Interactions between mother and positive affect [i.e. (own-mother positive > own-mother neutral) > (unfamiliar-mother positive > unfamiliar-mother neutral)] were found in the posterior cingulate, precuneus, rACC extending to dorsal ACC (dACC), and right ventrolateral PFC. The negative contrast of this interaction was associated with activation in the left anterior STS (Table 1 and Figure 3).

### Table 1 Mean (s.d.) of video-clip ratings completed post-MRI scan (n = 30)

<table>
<thead>
<tr>
<th>Clip</th>
<th>Own affect</th>
<th>Mother’s affect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Aggressive</td>
</tr>
<tr>
<td>Own mother</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Happy</td>
<td>54.6 (23.4)</td>
<td>22.2 (23.4)</td>
</tr>
<tr>
<td>Sad</td>
<td>10.7 (17.8)</td>
<td>26.4 (27.3)</td>
</tr>
<tr>
<td>Angry</td>
<td>10.5 (15.3)</td>
<td>35.1 (32.4)</td>
</tr>
<tr>
<td>Anxious</td>
<td>10.5 (18.9)</td>
<td>20.9 (26.2)</td>
</tr>
<tr>
<td>Unfamiliar mother</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Happy</td>
<td>53.6 (31.1)</td>
<td>18.5 (22.0)</td>
</tr>
<tr>
<td>Sad</td>
<td>4.3 (9.3)</td>
<td>20.1 (23.7)</td>
</tr>
<tr>
<td>Angry</td>
<td>8.5 (17.7)</td>
<td>25.0 (30.9)</td>
</tr>
<tr>
<td>Anxious</td>
<td>7.4 (11.5)</td>
<td>15.2 (20.8)</td>
</tr>
</tbody>
</table>

Fig. 1 Main effect of mother-positive affective behavior. Significant clusters overlaid on the MNI template brain (radiological format). $x = -48, y = -8, z = -10$

Fig. 2 Main effect of mother-aggressive affective behavior. Significant clusters overlaid on the MNI template brain (radiological format). $x = -50, y = -6, z = 20$. 
There was no activation associated with mother-aggressive affect interactions [i.e. (own-mother aggressive > own-mother neutral) > (unfamiliar-mother aggressive > unfamiliar-mother neutral)].

Mother–child relationship quality (indexed by frequency of mother aggressive behavior during the interactions), post-scan ratings of own emotional response to clips and perceptions of mothers’ emotion during clips were not.
associated with activation during positive or aggressive mother clips. Depressive symptoms, however, were negatively associated with rACC activity during own-mother positive behavior and mother positive behavior (main effect), respectively, showed a negative association with adolescent depressive symptoms.

(Table 2) Peak voxel coordinates (MNI space) for significant clusters, for each contrast

<table>
<thead>
<tr>
<th>Brain region</th>
<th>MNI coordinates&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Voxels</th>
<th>Z-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive &gt; neutral&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>64  -30</td>
<td>6</td>
<td>10603</td>
</tr>
<tr>
<td>L</td>
<td>-44 -42</td>
<td>0</td>
<td>5557</td>
</tr>
<tr>
<td>L occipital pole</td>
<td>-32 -98</td>
<td>-14</td>
<td>1642</td>
</tr>
<tr>
<td>R amygdala&lt;sup&gt;c&lt;/sup&gt;</td>
<td>22  -2</td>
<td>-20</td>
<td>4.56</td>
</tr>
<tr>
<td>Aggressive &gt; neutral&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>STS</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>R</td>
<td>64  -28</td>
<td>-4</td>
<td>5187</td>
</tr>
<tr>
<td>L</td>
<td>-62 -18</td>
<td>-4</td>
<td>5429</td>
</tr>
<tr>
<td>Temporal pole</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>R&lt;sup&gt;e&lt;/sup&gt;</td>
<td>44  18</td>
<td>-22</td>
<td>4.68</td>
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<tr>
<td>L&lt;sup&gt;e&lt;/sup&gt;</td>
<td>-41 14</td>
<td>-24</td>
<td>5.2</td>
</tr>
<tr>
<td>L occipital pole</td>
<td>-16 -96</td>
<td>-2</td>
<td>1506</td>
</tr>
<tr>
<td>R medial PFC&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4  56</td>
<td>16</td>
<td>3.65</td>
</tr>
<tr>
<td>L ACC</td>
<td>-10 28</td>
<td>12</td>
<td>630</td>
</tr>
<tr>
<td>Mother × positive interaction&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCC</td>
<td>0  -32</td>
<td>26</td>
<td>3426</td>
</tr>
<tr>
<td>R precuneus&lt;sup&gt;c&lt;/sup&gt;</td>
<td>8  -78</td>
<td>44</td>
<td>4.12</td>
</tr>
<tr>
<td>rACC</td>
<td>0  38</td>
<td>10</td>
<td>1400</td>
</tr>
<tr>
<td>L dorsal ACC&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-2</td>
<td>22</td>
<td>34</td>
</tr>
<tr>
<td>R ventrolateral PFC&lt;sup&gt;c&lt;/sup&gt;</td>
<td>36</td>
<td>30</td>
<td>-16</td>
</tr>
<tr>
<td>(−)Mother × positive interaction&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>L STS</td>
<td>-60 -22</td>
<td>-10</td>
<td>4.43</td>
</tr>
</tbody>
</table>

<sup>a</sup>Coordinates refer to the position (x, y and z mm) for the peak voxel in each cluster.

<sup>b</sup>Affective > neutral, collapsed across own- and unfamiliar-mother.

<sup>c</sup>Clusters in which more than one peak activation was detected.

<sup>d</sup>The negative of the interaction in <sup>c</sup>.

<sup>e</sup>(own-mother positive > own-mother neutral) > (unfamiliar-mother positive > unfamiliar-mother neutral).

(Figure 4). To probe what was driving this result, we investigated whether depressive symptoms were associated with activity for each simple contrast contributing to the interaction (i.e. own-mother positive > rest, own-mother neutral > rest, unfamiliar-mother positive > rest, unfamiliar-mother neutral > rest), using a 10 mm sphere over the rACC to mask the search area prior to thresholding results at $P < 0.001$, uncorrected. Depressive symptoms were negatively associated only with rACC activity for the own-mother positive > rest contrast.

Depressive symptoms were also negatively associated with activity in the right putamen ($x=32$, $y=-8$, $z=-6$; voxels = 10, $Z=3.61$, Figure 4) and lateral occipital cortex ($x=44$, $y=-86$, $z=-8$; voxels = 37, $Z=3.93$) during exposure to positive affective behavior in general (i.e. positive > neutral, collapsed across own- and unfamiliar-mother).

DISCUSSION

Using a novel paradigm that employed personally relevant ecologically valid stimuli, we found that exposure to adolescents’ own mother’s positive affective behavior (relative to an unfamiliar mother’s positive behavior) was associated with adolescent brain activation in the anterior and posterior cingulate, precuneus and ventrolateral PFC. In contrast, exposure to positive affective behavior in general (i.e. across one’s own and an unfamiliar mother) was associated with brain activation in the STS, occipital pole, amygdala, hippocampus and striatum. While adolescents’ own-mother aggressive behavior was not associated with brain activation relative to an unfamiliar mother’s aggressive behavior, exposure to aggressive behavior in general was associated with brain activity in the STS, occipital pole, ACC and thalamus. Further, we found that adolescent depressive symptoms were associated with reduced rACC activity during own-mother positive behavior, and reduced striatal and lateral occipital activity during positive affective behavior in general.

Our innovative task allowed us to investigate adolescent neural activation distinctively associated with exposure to their own mother’s affective behavior. Examining the interaction between mother (own vs unfamiliar) and affect (aggressive/positive vs neutral) allowed us to probe neural...
function that could not be explained by either familiarity or affect in general. We found that the interaction for positive behavior was associated with activation in the PCC, precuneus, rACC extending to dACC, and right ventrolateral PFC. Both the rACC and PCC have been implicated in positive emotion (Paradiso et al., 1999; Bartels and Zeki, 2000; Rolls et al., 2003). Indeed, a meta-analysis of 23 functional imaging studies showed that compared to other emotions, positive emotion processing was specifically localized to these two regions of the cingulate (Vogt, 2005). Interestingly, for the rACC there was relatively more activation associated with positive compared to neutral behavior for one’s own mother, whereas activation in the same region was relatively greater for neutral compared to positive behavior for the unfamiliar mother. It is notable that positive stimuli have been associated with both rACC increases and decreases (Gotlib et al., 2005). The majority of studies finding increased rACC activity (relative to a baseline condition) have been in the context of reward or happy mood (Vogt, 2005), whereas decreased activation has been found mainly in the context of perceptual tasks involving positive stimuli (i.e. where mood was not directly manipulated) (Gotlib et al., 2005). Further, it has been found that while emotional tasks requiring exteroception are associated with reduced rACC activity, emotional tasks requiring more introspective modes of processing are associated with increased rACC activity (Grimm et al., 2009). This is somewhat consistent with the identified role of both the rACC and PCC in the brain’s default mode network, whose activity is thought to decrease during cognitively demanding tasks, and whose increased activity is thought to reflect self-referential processing that is hypothesized to provide a means to anticipate and evaluate future events (Buckner et al., 2008). Thus, increased activity in these regions for the own-mother condition might reflect intrinsic reward or anticipation of reward and/or greater interoceptive or self-referential processing, whereas decreased activity associated with the unfamiliar mother might reflect exteroceptive or increased cognitive processing.

The ventrolateral PFC has been implicated in the self-regulation of emotion (Ochsner and Gross, 2005). Given that activation of this region associated with the interaction contrast appeared to be driven by deactivation for the unfamiliar mother’s positive relative to neutral behavior, it may be that this finding reflects a disinhibition of emotional self-regulation for the unfamiliar mother positive clips. This may be because participants’ found the unfamiliar mother’s positive behavior particularly engaging, and thus were less aware (consciously or unconsciously) of the need to regulate their own emotional responses (indeed, participants rated the unfamiliar mother as being more happy than their own mother for the positive behavior clips).

The precuneus, in addition to playing a key role in autobiographical memory (Cavanna and Trimble, 2006), has been suggested to be involved in emotion attribution (Ochsner et al., 2004), which may account for our finding of increased activation in this region during own-mother positive behavior. However, it is noted that a prominent decrease in precuneus activation for unfamiliar-mother’s positive behavior seemed to drive the significant result for the interaction contrast. Given that the precuneus is also part of the brain’s default mode network, it is possible that our finding reflects increased cognitive load (and decreased self-referential processing) associated with processing the novel unfamiliar-mother positive clips.

Although we did not see increased striatal activation for the mother positive interaction, we did find activation in the putamen (i.e. dorsal striatum) during adolescent exposure to positive affective behavior in general (i.e. across own- and unfamiliar-mother clips), consistent with the recently described role of this region in reward processing (Corbit and Janak, 2010). Exposure to positive behavior in general was also associated with adolescent neural activation in regions associated with facial emotion processing (such as the STS, Narumoto et al., 2001), and attention to arousing emotional stimuli (such as the occipital pole, Norris et al., 2004). Positive behavior was also associated with amygdala activation, which is consistent with emerging evidence that the amygdala plays a key role in the perception of positive emotional stimuli (Yang et al., 2002), and is also thought to play a crucial role in reward learning (Baxter and Murray, 2002).

That no activations were associated with the mother aggressive interaction is surprising, given that aggressive parenting behavior has been found to influence adolescents’ affective behavior and adjustment (Fauber et al., 1990). Given that the fMRI was performed ~4.5 years after the video footage was collected, it may be that the adolescents’ own mother’s aggressive behavior was not highly salient and the contentious issues discussed during the interaction may have been resolved, or were now developmentally irrelevant (e.g. conflict regarding a curfew). Exposure to aggressive behavior in general (i.e. across own- and unfamiliar-mother clips), however, was associated with adolescent neural activity in a number of regions, including the STS and occipital pole (similarly to positive affective behavior), the medial PFC/rACC and the thalamus. A role for the medial PFC/rACC in responding to threat is supported by previous research showing that activation in this region is associated with exposure to angry facial expressions (Blair et al., 1999), and it has been suggested that such activity might be associated with emotional experience and/or increased attention (Lane et al., 1998). The thalamus is thought to have a key role in regulating arousal and awareness and has strong afferent connections to the medial PFC (Vertes, 2006). Our finding is consistent with other research showing increased thalamic activity during the experience of unpleasant emotion and arousal (Lane et al., 1997; Anders et al., 2004). The fact that we observed a main effect of aggressive behavior, but not an interaction between the mother (own vs unfamiliar mother) and aggression, while such an
interaction was found for positive behavior, also suggests the possibility that neural responses to aggressive behavior are not moderated by familiarity or kin relatedness as much as are neural responses to positive behavior, perhaps because of the distinctive evolutionary and developmental significance of warmth and attachment within maternal-child interactions (Bora et al., 2009).

It is notable that a number of brain regions found to show greater activation during exposure to mother affective behavior, including the STS, precuneus and rACC, are known to be involved in theory of mind (i.e. the ability to attribute mental states, such as feelings, beliefs and intentions, to oneself and others, Blakemore et al., 2007). The STS was activated for both positive and aggressive behavior across the own- and unfamiliar-mother clips. As mentioned above, the STS is thought to be involved in facial emotion processing, an important and necessary ability for mentalizing about the internal states of others. The rACC and precuneus were both activated to a greater extent to own-mother compared to unfamiliar-mother positive behavior. While both regions have been implicated in theory of mind, they have been particularly implicated in thinking about mental states in relation to the self (Lou et al., 2004; Ochsner et al., 2004).

Thus, it is possible that these regions were more active in adolescents while watching their own (compared to an unfamiliar) mother's positive behavior because they were reflecting on their own thoughts and feelings to a greater extent. This may be because their own mother's affective behavior provides important feedback that shapes the way adolescents regulate their own emotions and behavior (Yap et al., 2008).

**Depressive symptoms**

Adolescent depressive symptoms correlated negatively with activity in the rACC during own-mother positive behavior clips. As mentioned above, this brain region has been implicated in the experience of positive emotion (Vogt, 2005) and in reward (Ongur and Price, 2000; Forbes et al., 2010). While some studies have reported increased activity in this region during exposure to positive stimuli in depressed participants, it is noted that these positive associations have been found in the context of normative decreases in activity for healthy controls (Gotlib et al., 2005; Harvey et al., 2007). As mentioned above, normative decreases in this region during exposure to generic positive stimuli might underlie increases in effortful cognitive processing of external stimuli, and thus an increase in activity in this region in depressed patients relative to controls might indicate a lack of attentional resources directed towards the positive stimuli. In our paradigm, the association between increased depressive symptoms and decreased rACC activity (in contrast to normative increases during exposure to mother positive behavior) might indicate that own-mother positive behavior was associated with reduced self-referential processing, or reduced experience of reward or happiness in the adolescents with higher depressive symptoms. This latter idea is consistent with other research showing depression to be associated with decreased ACC activity during reward processing (Forbes et al., 2006). Further, although adolescents’ ratings of their own affect and perception of mother affect were not associated with brain activity during the task, it is of note that depressive symptoms were associated with a tendency to report greater levels of negative affect during the positive clips. Thus, these findings offer some insight into the mechanisms by which adolescents’ reactivity to their mother’s emotional behavior might contribute to increased depressive symptoms. In particular, dysfunctional reward-related neural function associated with perception or reactivity to one’s mother’s positive behavior may contribute to increased depressive symptoms in adolescents. It is also possible that the quality of the mother–child relationship was driving the association between depressive symptoms and brain function. For example, adolescents who experience lower quality relationships might show both higher depressive symptoms and abnormal brain function. While we found that higher depressive symptoms were associated with lower relationship quality (i.e. higher frequency of mother aggressive behavior during the videotaped interactions), relationship quality was not associated with neural activity for the mother positive behavior clip. This suggests that the depression-related neural activity is more likely to be associated with the adolescent’s subjective interpretation or emotional response to the clip.

During exposure to positive affective behavior in general (i.e. across own- and unfamiliar-mother clips), adolescent depressive symptoms were also negatively associated with activity in the putamen. This finding is consistent with other research showing that depressed individuals, and individuals at risk for depression, exhibit hypoactivation in this region during exposure to pleasant visual stimuli (Surguladze et al., 2005), and reward anticipation and experience (Forbes et al., 2009a; Gotlib et al., 2010). Our finding might reflect dysfunctional reward processing in adolescents with higher depressive symptoms. Given that our participants with high current depressive symptoms also had a history of high depressive symptoms and that this trajectory has been identified as a risk factor for depressive disorder and other adverse outcomes, it may be that abnormal functioning of the rACC and putamen (particularly associated with positive emotion processing) contributes to this risk.

**Strengths and limitations**

The use of dynamic personally relevant stimuli is a major strength of the study. However, it must be noted that the use of this type of stimuli has its limitations, such as the complex nature of the stimuli, and lack of true standardization. Although we controlled for mother neutral behavior in all analyses, minimizing a number of confounding effects, the own- and unfamiliar-mother clips differed on a number of
points, including the fact that the adolescents were present at the time of filming the own mother footage.

Further, while we did match own- and unfamiliar-mother clips on valence (categorically), the coding system used does not currently include continuous intensity ratings. Thus, we were unable to match these clips on intensity, and given that the unfamiliar-mother positive and negative clips were rated by the adolescent as more happy and angry, respectively, it is possible that the unfamiliar-mother clips were of a higher intensity. While this might have contributed to a lack of significantly greater brain activation associated with own vs unfamiliar mother aggressive affect, that we found significantly greater brain activation associated with own vs unfamiliar mother positive affect (when own-mother positive clips were potentially less intense) is notable. Nonetheless, future work should investigate the effects of objectively rated affective intensity of maternal behavior on neural activation.

It is also of note that while inter-rater reliability estimates for the construct codes used to classify mother affective behavior were all considered high, there is always a level of subjectivity in observational measures and it is likely that this subjectivity introduces some error that may constrain effects.

A further strength of the study is the narrow age range of participants. This is in contrast to the majority of adolescent studies that often include samples of adolescents whose ages span a number of years. This approach is problematic given the marked development of brain structure and function that occurs across the adolescent period (Durston et al., 2006). It is of further note that the current sample comprised individuals at a fairly late stage of adolescence (i.e. 17-year olds). It is unknown whether the current results would translate to a younger group of adolescents, however, given that early (i.e. peripubertal) adolescence is associated with (i) marked brain development (Nelson et al., 2005), (ii) a dip in some cognitive functions (McGivern et al., 2002) and (iii) marked changes in social relationships (e.g. engagement in more peer relationships, Nelson et al., 2005), the underlying neural processes are likely to be different.

Another limitation is that the own mother footage was collected, on average, 4.5 years prior to this study, calling into question the relevance of the stimuli to the adolescent at the time of the MRI scan. However, adolescents’ own affect (as assessed via self-report) was successfully manipulated in the directions expected, indicating that the own-mother clips were still eliciting affective responses years later. Further, the external classification of the affective behavior in all clips was found to be verified by the adolescent’s own report.

Another limitation to note regarding the use of such complex stimuli is that it is difficult to infer the underlying processes contributing to the observed brain activation. Although we speculate that neural activation was associated with emotional experience, it might also relate to emotion perception or emotion regulation, for example. We attempted to probe the meaning of the observed neural activation by investigating associations with (i) subjective reports of own and mother affect, and (ii) objective measures of the quality of the mother–child relationship, but we did not find any significant relationships. It is of note, however, that subjective and objective measures of emotional experience or perception often diverge (Gross et al., 1993), and that individuals may not be accurate in reporting their own emotional processes (Robinson et al., 2002). Thus, we cannot be sure that neural activation was not associated with subjective experience or perception of affect. We suggest that further research employing other objective indices, such as physiological response, might be useful to further probe the exact meaning of the neural activation observed and its relation to depressive symptoms.

Since no behavioral response was required from participants during scanning, we cannot comment on the extent to which adolescents attended to the stimuli. Although each clip had repeated presentations, given the nature of the stimuli (evocative affective video clips), it is reasonable to assume that lack of attention was not a significant issue.

Investigation of depressive symptoms during adolescence is advantageous due to the clinically important trajectories of symptom change occurring during this developmental phase, and the well-established relationship between increasing symptoms and later disorder (Dekker et al., 2007; Shankman et al., 2009; Kovacs and Lopez-Duran, 2010). Thus, focusing on symptoms allows us to make inferences about possible risk processes. However, it would be of interest for future work to test this paradigm in a clinically depressed adolescent sample to examine the effects of case-level disorder on social–emotional brain function.

CONCLUSIONS

This study represents one of few investigations into adolescent affect-related neural function using ecologically valid personally relevant affective stimuli. We found that exposure to adolescents’ own mother’s affective behavior was associated with activation in brain regions implicated in emotion processing, social cognition and self-referential processing. These findings contribute to our understanding of the neurobiology of adolescent affective processing in realistic and personally relevant environmental contexts. Our findings also suggest that abnormal processing of positive interpersonal emotional stimuli in the rACC and putamen (which may reflect reduced experience of reward or positive affect) is associated with depressive symptoms during adolescence, and may represent a vulnerability factor for the development more severe depressive and other mental health outcomes later in life.

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Conflict of Interest

None declared.

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