Anxiously elaborating the social percept: Anxiety and age differences in functional connectivity of the fusiform face area in a peer evaluation paradigm

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Abstract

Objectives: Social anxiety disorder involves biased cognition and altered neural responses to social stimuli. This study further assesses the precise ways in which neural activation associated with perceptual processing of faces differs in socially anxious and non-anxious individuals. Method: Functional magnetic resonance imaging data were acquired as 90 anxious or healthy juveniles and adults performed a peer feedback task. Psychophysiological functional connectivity analysis was performed on all participants using a seed placed in the right fusiform face area (rFFA). Results: Social anxiety was associated with enhanced rFFA coupling in several areas of ventral visual stream when viewing feedback from peers previously rejected by participants; healthy participants demonstrated the opposite pattern. Moreover, anxious juveniles had greater positive rFFA coupling with right inferior temporal gyrus during feedback from rejected peers; other groups showed the opposite pattern. Finally, anxious juveniles had greater positive rFFA coupling with pregenual anterior cingulate cortex during negative peer feedback; other groups displayed the opposite pattern. Conclusions: Anxious individuals, and juveniles in particular, may dedicate more neural resources to stimuli associated with potentially negative, relative to positive, social outcomes; non-anxious individuals may do the opposite.

Key words: development, face perception, psychophysiological interaction, social anxiety

What is already known about this topic?

2. Neural processing of stimuli involves multiple stages of elaboration.
3. Anxiety expression changes over the course of development.

What this topic adds?

1. Anxiety is associated with aberrant weighting of perceptual processing of relevant stimuli in regions of the core and extended face perception network.
2. Memory and brain responses may be a tractable and malleable index of cognitive bias.
3. Marked developmental differences in anxious populations may reflect age differences in how biases manifest.

Social anxiety disorder (SAD) typically emerges in adolescence and manifests as excessive worry and social avoidance (Stein & Stein, 2008). Many cognitive biases have been linked with SAD (Roth & Heimberg, 2001), and recently functional neuroimaging has enabled assessment of the neural mechanisms underlying these processes (Haller, Cohen Kadosh, Scerif, & Lau, 2015). Functional neuroimaging studies in SAD suggest perturbed processing of social stimuli in a variety of regions related to processing at both...
affective and cognitive levels (Brühl, Delsignore, Komossa, & Weidt, 2014; Freitas-Ferrari et al., 2010; Goldin, Manber, Hakimi, Canli, & Gross, 2009; Geyer et al., 2014; Jarcho et al., 2015; Phan, Fitzgerald, Nathan, & Tancer, 2006; Richey et al., 2014; Spielberg et al., 2015).

While brain imaging has long focused on functioning in particular regions, recent approaches target functional networks, which may help illuminate how information is integrated across the brain (O’Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012). Several such studies in SAD have reported differential connectivity patterns between the prefrontal cortex (PFC) and subcortical structures like the amygdala and striatum (Ding et al., 2011; Hahn et al., 2011; Liao et al., 2010; Miskovic & Schmidt, 2012; Prater, Hosanagar, Klumpp, Angstadt, & Phan, 2013). These differences are thought to reflect altered integration of socio-emotional experiences with executive processes in SAD (Jarcho et al., 2015; Nelson & Guyer, 2011).

In addition to dysfunction in affective and cognitive brain network interactions, differential integration between perceptual networks and other brain systems may also underlie SAD (Büchel & Friston, 1997; Pehrs et al., 2015). This study assesses functional connectivity differences in the fusiform face area (FFA), a relatively early node of the face perception network (Kanwisher, McDermott, & Chun, 1997; Weiner & Grill-Spector, 2012), as a function of age and anxiety. Although the FFA is a region that demonstrates rapid and specific activation in response to faces, it also receives extensive ‘back projection’ from regions in limbic and prefrontal areas (Brühl et al., 2014). At a functional level, this back projection likely amplifies neural signalling elicited by a specific face and enhances processing of the facial percept. This may manifest in a number of ways, including increased attention and greater recall (Baldauf & Desimone, 2014; Hasinski & Sederberg, 2016).

Prior studies find that anxiety relates to reduced negative functional connectivity between face-selective regions of the fusiform gyrus and posterior cingulate, precuneus, and sensorimotor regions; reduced positive coupling of the fusiform with ventromedial PFC; and increased positive coupling with the amygdala (Danti et al., 2010; Frick, Howner, Fischer, Kristiansson, & Furmark, 2013). Most of these studies examine global patterns of connectivity rather than context-specific differences. Several studies also find differences in FFA connectivity patterns as a function of normative development, generally noting an overall increase in size and more task-based flexibility in seed-based FFA networks (Cohen Kadosh, Johnson, Dick, Cohen Kadosh, & Blakemore, 2013; Golarai, Liberman, Yoon, & Grill-Spector, 2010; Scherf & Scott, 2012). We are aware of no study examining FFA connectivity in anxiety and development concomitantly.

This study compares FFA connectivity between socially anxious and non-anxious juveniles and adults using the Chatroom Task, in which participants select or reject peers for an online chat and receive peer feedback (see Jarcho et al. (2015); Spielberg et al. (2015) for prior reports using this dataset). Previous functional connectivity analyses of Chatroom data have placed seeds in the amygdala and striatum and reveal differential connectivity with the PFC as a function of both anxiety and development (Guyer et al., 2008; Jarcho et al., 2015; Spielberg et al., 2015). These findings link SAD to perturbed processing of salient social information and further suggest that perturbations may manifest differently in juveniles and adults.

By using an FFA seed, we mapped the ways in which brain regions differentially modulate activation of face perception across anxiety and development. A variety of cognitive biases associated with SAD, including biases in attention, perception, interpretation, or memory, could conceivably manifest in the context of the Chatroom Task. As our seed was placed in a region associated with face perception, we expected to find evidence of perceptual biases, but we also expected we might find differential connectivity with neural systems that interact with the face perception network, such as those underlying attention, interpretation, and memory. As with previous findings, we predicted that differential coupling between the FFA and other regions would emerge as a function of both participants’ selection of peers for a potential social interaction and type of feedback received. We further predicted interactive effects between age group and anxiety status due to the increased salience of peers and the ongoing developmental processes during adolescence (Blakemore & Mills, 2014). As functional localisation studies have found activations specific to faces more consistently and of greater magnitude in the right fusiform (Haxby, Hoffman, & Gobbini, 2000; Kanwisher et al., 1997), we restrict our attention to the right FFA (rFFA).

METHODS

Participants

Participants consisted of 90 clinically anxious and psychiatrically healthy juveniles and adults recruited from the local community. Following initial screening, participants underwent a semi-structured clinical interview performed by a trained clinician (masters or above). All anxious participants met DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) criteria for anxiety, and although only 82% of anxious participants met full DSM-IV criteria for SAD, all expressed clinically significant levels of fear of social situations in diagnostic interviews or scales (score >20 on Fear of Negative Evaluation (Watson & Friend, 1969) or >40 on Liebowitz Social Anxiety Scale (Liebowitz, 1987)). Exclusion criteria required that all participants be free of selective serotonin reuptake inhibitor (SSRI) use for at least
one month and must not have been treated with an SSRI for their current episode. All participants were free of psychoactive medication at time of testing. Demographics of the four groups are depicted in Table 1.

Chatroom Task

The Chatroom Task has been described in detail previously (Guyer, McClure-Tone, Shiffrin, Pine, & Nelson, 2009; Guyer et al., 2008, 2014; Jarcho et al., 2015; Lau et al., 2011; Spielberg et al., 2015). The task requires that participants make two visits to the lab, separated by approximately 2 weeks. On the initial visit, participants were told that the task is a multi-site study designed to assess how individuals interact with previously unknown people on the internet. Participants were then shown an array of 60 photographs of other age-matched (within age categories 8–11, 12–14, 15–17, or 18+ years, equal numbers male and female) peers, who, they were told, were other participants in the study. Participants sorted these photos into two equal-sized groups representing peers they would and would not want to have an online chat with on a subsequent visit. A photograph was then taken of the participant, and they were told that other participants in the study would be shown this rating and then rate their photograph in a similar manner.

After approximately 2 weeks (M = 11.87, SD = 7.42 days), participants returned for a functional magnetic resonance imaging (fMRI) scan. The Chatroom Task was divided into two runs. In the first run (not considered here), participants predicted how much the peer depicted in each photograph liked them. In the second run, the peers’ ratings were revealed (Fig. 1). Trials in the second run were divided into two phases. Initially, each face was displayed for 3 s, and participants were reminded how they rated this person previously (e.g., ‘you were interested’ or ‘you were not interested’). This anticipation phase was followed by a

![Figure 1](https://example.com/figure1.png)

**Figure 1** The Chatroom Task consists of two visits to the lab. On the initial visit (top), participants view 60 unknown age-matched peers and sort them into two equal-sized groups based on future desire to engage in an online chat. The participants then have their own photograph taken and are told other participants will rate them in a similar manner. On the subsequent visit (middle), participants view how others sorted them while undergoing functional neuroimaging. Finally, immediately after the scan, participants are asked to recall the type of feedback they received from each peer (bottom).

| Table 1 Demographics | Juveniles | | | | | | Adults | | | |
|-------------------|----------|----------|----------------|----------|----------|----------|----------|----------|----------|----------|----------|
|                    | Non-anxious | Anxious | p value | Non-anxious | Anxious | p value |
| N                  | 24        | 15       |         | 32        | 19       | .055     |
| Female (%)         | 38        | 60       |         | 53        | 79       | .633     |
| Age (years)        | 13.7 (2.4)| 12.8 (3.4)| .435 | 26.2 (5.2)| 27.8 (7.8)| .363 |
| Age range          | 9.4–17.2  | 8.0–17.4 |         | 21.0–44.8 | 18.3–49.6 |         |
| IQ                 | 112.6 (11.7)| 104.8 (12.5)| .035 | 119.1 (11.4)| 112.8 (12.6)| .031 |
| FNE                | 6.9 (5.0) | 21.1 (8.3) | <.001 | 9.8 (4.9) | 22.1 (8.1) | <.0001 |
| SCARED<sup>a</sup> | 5.3 (5.4) | 34.0 (6.9) | <.0001 | —         | —        | —       |
| Scanner 1 (%)      | 42        | 13       |         | 38        | 11       | .047     |

Notes. Values are mean (SD) unless otherwise specified. All p values were derived from Wilcoxon rank-sum test with continuity correction and involved comparisons within age groups, with the exception of per cent female and per cent scanner 1, which used Fisher's exact test and compared proportions across all four groups. Missing data: IQ: 1 anxious adult; FNE: 1 non-anxious juvenile, 2 anxious juveniles, 4 anxious adults. IQ = intelligence quotient; FNE = Fear of Negative Evaluation; SCARED = Screen for Child Anxiety Related Disorders.

<sup>a</sup>Average of juvenile and parent SCARED evaluations.
feedback phase, in which the words ‘they are interested’ or ‘they are not interested’ was overlaid on the face (2 s). After the feedback was revealed, participants rated their expectation of the outcome (3–5 s). Equal numbers of positive and negative feedback trials were presented, and the order was randomised. A fixation jitter of 0–8 s was interspersed between the anticipation and feedback phases to decouple events in time. Finally, in order to assess potential memory biases, immediately after the neuroimaging session, a surprise memory test was administered where participants were asked to recall the responses of each peer.

Data processing and analysis

Data processing and analysis was conducted with AFNI software (Cox, 1996) and R version 3.2.2 (R Core Team, 2015). Standard fMRI acquisition and preprocessing methods were used (see Supporting Information).

Seed identification

Individual-level general linear models (GLMs) were fit with six task regressors corresponding to the face perception events of the anticipation and feedback phases of the Chatroom Task; two anticipation regressors represented participant selection and rejection of peers on the initial visit, and four feedback regressors represented the crossing of participant selection (‘selected peer feedback’ and ‘rejected peer feedback’) and type of feedback received (‘positive peer feedback’ and ‘negative peer feedback’). Events were modelled with BLOCK basis functions of the appropriate event duration and convolved with the hemodynamic response function included in AFNI. Models also included six motion regressors and seven orthogonal polynomials to account for head motion and low-frequency drift in the fMRI signal, respectively.

An initial one-sample t-test (3dttest++ in AFNI) was performed on data grouped from all participants to identify the area of maximal response to faces in the right fusiform gyrus. The voxel in the right medial fusiform gyrus with the highest t-value for task-baseline contrast (mean per cent signal change = 0.54; t(89) = 16.20; uncorrected p = 6.0 × 10−28; Talairach coordinates 34, −44, −19) was chosen as the centre of the 6-mm radius sphere defining the rFFA. The average task versus baseline contrast value across all voxels in the rFFA sphere was extracted for each participant, and these values were subjected to a two-way between-subjects sequential sum of squares analysis of variance (ANOVA). The results indicate no significant effect of anxiety diagnosis (F(1, 86) = 0.56, p = .457), age group (F(1, 86) = 0.77, p = .384), or their interaction (F(1, 86) = 1.63, p = .205), and comparable levels of rFFA activation across groups (F(3, 86) = 0.99, p = .403) (Fig. 2).

Task-dependent functional connectivity analyses

We next performed psychophysiological interaction (PPI) connectivity analyses (Friston et al., 1997; O’Reilly et al., 2012) using the rFFA seed. Six PPI regressors corresponding to the six event types were created for each participant; they function essentially as interaction terms that cross the expected BOLD response time intervals associated with each event type with the individual participants’ rFFA seed region time series. A group-level whole-brain PPI analysis (3dMVM in AFNI; Chen, Adleman, Saad, Leibenluft, and Cox (2014)) modelled the four PPI feedback coefficient estimates in a repeated measures ANOVA, including between-subject factors age group, diagnosis group, their interaction; within-subject factors participant selection, peer feedback, their interaction; interactions between all between- and within-subject factors; and fMRI scanner as a between-subject factor.

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Figure 2  The right fusiform face area (rFFA) region of interest applied to all participants is depicted by the red sphere overlaid on the structural MRI images (left). The mean (± SEM) task per cent signal change (relative to baseline) across groups is depicted in the bar graph (right).
of no interest. The two anticipation PPI coefficients were not of interest for the current analysis, so they were not included in the group model to conserve statistical power. Because of the low sensitivity of PPI (O’Reilly et al., 2012), voxel-wise significance threshold was set to \( p < .005 \), with a minimum cluster size of 50 voxels. This is similar to other connectivity analytical approaches (Frick et al., 2013; Jarcho et al., 2015).

For statistically significant interactions involving both a within-subject factor and diagnosis group, for each participant, we extracted the mean of each of the four PPI coefficient estimates over all voxels in the regions that survived the significance threshold and calculated the appropriate within-subject contrasts (selected peer feedback–rejected peer feedback and positive peer feedback–negative peer feedback). For interactions that only involved a within-subject factor and diagnosis group, we performed Welch’s \( t \)-test on the extracted data contrasts to confirm significant differences across diagnosis. To control for potential confounding by group differences in baseline covariates, we then fit linear regression models controlled by continuous age, gender, IQ, and scanner. For interactions that additionally involved age group, we fit two-way between-subjects ANOVA models to the extracted data contrasts, including diagnosis group, age group, and interaction terms, and performed post hoc Bonferroni-corrected pair-wise comparisons (Welch’s \( t \)-test) of group means (six comparisons). We then adjusted the ANOVA models by gender, IQ, and scanner. We also tested the association of the extracted data contrasts with continuous age via linear regressions, unadjusted and adjusted for positive, negative, and scanner. We examined the expectancy rating and memory data alone by calculating analogous within-subject contrasts (e.g., memory per cent correct for positive peer feedback–memory per cent correct for negative peer feedback) and modelled these using two-way between-subjects ANOVA with diagnosis, age group, and interaction terms. We then assessed the association of the memory contrasts with corresponding extracted data contrasts using linear regression.

**RESULTS**

Several brain regions differed significantly in task-dependent rFFA functional connectivity across anxiety, some of which also interacted with age group (Table 2). Because the focus of this article is on anxiety and development, we highlight differences that varied as a function of diagnosis or in which diagnosis and age group interacted. Several other significant findings also emerged (see Table S1, Supporting Information).

In four regions, task-dependent differences emerged as a function of anxiety. Three of these regions were in the occipital lobe, and one was in the cerebellum (Table 2, Fig. 3). Because the cerebellar regions have not been associated with either perceptual processing or anxiety, they will not be considered further. The three occipital regions displayed similar patterns of task-based connectivity differences. For non-anxious participants, greater positive coupling was found between the occipital regions and the rFFA during feedback from previously selected, relative to rejected, peers regardless of the type of feedback. Conversely, anxious participants had greater positive coupling with rFFA during feedback from rejected, relative to selected, peers. These group differences remained after

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### Table 2: Task-dependent functional connectivity of the right fusiform face area during feedback in the Chatroom Task

<table>
<thead>
<tr>
<th>Region</th>
<th>Voxels</th>
<th>( x )</th>
<th>( y )</th>
<th>( z )</th>
<th>( F(1, 84) )</th>
<th>( p ) value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis ( \times ) participant selection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left cuneus/lingual gyrus</td>
<td>290</td>
<td>−11</td>
<td>−71</td>
<td>−14</td>
<td>14.12</td>
<td>( &lt;10^{-3} )</td>
</tr>
<tr>
<td>Right cerebellum</td>
<td>105</td>
<td>51</td>
<td>−44</td>
<td>−36</td>
<td>27.06</td>
<td>( &lt;10^{-5} )</td>
</tr>
<tr>
<td>Right declive (OFA)</td>
<td>81</td>
<td>29</td>
<td>−61</td>
<td>−16</td>
<td>15.88</td>
<td>( 10^{-4} )</td>
</tr>
<tr>
<td>Left declive (OFA)</td>
<td>55</td>
<td>−29</td>
<td>−64</td>
<td>−16</td>
<td>19.24</td>
<td>( &lt;10^{-4} )</td>
</tr>
<tr>
<td>Age group ( \times ) diagnosis ( \times ) participant selection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left cerebellum</td>
<td>234</td>
<td>−4</td>
<td>−56</td>
<td>−36</td>
<td>16.15</td>
<td>( 10^{-4} )</td>
</tr>
<tr>
<td>Right inferior temporal gyrus</td>
<td>55</td>
<td>41</td>
<td>−4</td>
<td>−36</td>
<td>24.86</td>
<td>( &lt;10^{-5} )</td>
</tr>
<tr>
<td>Diagnosis ( \times ) peer feedback</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No suprathreshold activations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group ( \times ) threshold ( \times ) peer feedback</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left anterior cingulate</td>
<td>61</td>
<td>−4</td>
<td>36</td>
<td>6</td>
<td>15.38</td>
<td>( &lt;10^{-3} )</td>
</tr>
</tbody>
</table>

Notes. Voxel-wise \( p < .005 \), cluster threshold of 50 voxels; coordinates are for maximum \( F \)-value. Significant differences across diagnosis group. OFA = occipital face area.

*Uncorrected.
controlling for continuous age, gender, IQ, and scanner differences across groups (all \( p < .005 \), Table S2).

There were two regions where an interaction between anxiety and age group was found in rFFA coupling: one in the right inferior temporal gyrus (rITG) and the other in the cerebellum (Table 2, Fig. 4). In the inferior temporal lobe, anxious juveniles exhibited greater positive coupling with the rFFA during feedback from previously rejected peers, whereas all other groups displayed greater positive coupling with previously selected peers. Pair-wise comparisons of extracted data indicated that the mean contrast (selected peer feedback–rejected peer feedback) for anxious juveniles was significantly lower than those for the other groups (Bonferroni-adjusted \( p < .05 \)), while the other groups did not significantly differ from each other (Bonferroni-adjusted \( p > .05 \)). ANOVA analyses revealed a significant age group by diagnosis interaction both before \((F(1, 80) = 19.09, p < .001)\) and after adjusting for gender, IQ, and scanner \((F(1, 77) = 20.09, p < .001; \text{Table S3A})\). Unadjusted linear regressions against continuous age resulted in a non-significant negative slope in rITG–rFFA connectivity for the non-anxious group \((t(49) = -1.42, p = .163)\) and a significant positive slope for the anxious group \((t(31) = 4.87, p < .001)\). These results remained similar after controlling for gender, IQ, and scanner and were robust to outlier sensitivity analyses for the anxious group (Table S3B, Fig. 4).

Finally, another three-way interaction was found as a function of peer feedback (collapsed across participant selection at initial visit). A region in the left pregenual anterior cingulate cortex (lACC) exhibited relatively greater rFFA connectivity to negative than positive feedback in anxious juveniles, but other groups displayed greater connectivity during positive feedback (Table 2, Fig. 5). Pair-wise comparisons of extracted data indicated that the mean contrast (positive peer feedback–negative peer feedback) for anxious juveniles was significantly lower than for non-anxious juveniles (Bonferroni-adjusted \( p = .022 \)) and anxious adults (Bonferroni-adjusted \( p = .016 \)), but not significantly different from non-anxious adults (Bonferroni-adjusted \( p = .163 \)). The other group means did not significantly differ.
from each other (Bonferroni-adjusted \( p > .05 \)). ANOVA analyses revealed significant age group by diagnosis interaction both before (\( F(1, 86) = 16.61, \ p < .001 \)) and after adjusting for gender, IQ, and scanner (\( F(1, 83) = 15.36, \ p < .001 \); Table S4A). Unadjusted linear regressions against continuous age resulted in a non-significant negative slope in lACC–rFFA connectivity for the non-anxious group (\( t(54) = -1.40, \ p = .167 \)) and a significant positive slope for the anxious group (\( t(32) = 2.16, \ p = .038 \)). Results were similar after controlling for gender, IQ, and scanner (Table S4B, Fig. 5).

Lastly, we analysed the expectancy rating and memory data alone and the memory data in relation to functional connectivity findings. A two-way sequential sum of squares ANOVA performed on the expectancy rating peer feedback contrast revealed a significant effect of anxiety diagnosis (\( F(1, 86) = 4.43, \ p = .038 \)) but no main effect for age group (\( F(1, 86) = 0.60, \ p = .442 \)) or age group by diagnosis interaction (\( F(1, 86) = 0.82, \ p = .367 \)). We found a similar result for the memory peer feedback contrast: ANOVA revealed a significant effect of anxiety diagnosis (\( F(1, 85) = 4.80, \ p = .031 \)) but no main effect for age group (\( F(1, 85) = 1.23, \ p = .270 \)) or age group by diagnosis interaction (\( F(1, 85) = 0.45, \ p = .506 \); one non-anxious juvenile with missing memory data was excluded from the memory analyses). Thus, anxious participants were more likely to expect negative than positive feedback and were more biased to accurately remember negative peer feedback events than were non-anxious participants. These measures were significantly positively correlated in a univariate regression (\( r^2 = .07, \ p = .010 \)). Neither the expectancy rating nor the memory data showed any significant group differences in the participant selection contrasts. In an exploratory analysis of all significant regions discussed above, only

Figure 4  A region of the right inferior temporal gyrus (rITG) exhibited a significant age group by diagnosis interaction for the participant selection contrast (overlaid on structural images at left). Graphs at the top show mean (± SEM) right fusiform face area (rFFA) connectivity during selected and rejected peer feedback (top left) and mean (± SEM) contrast of selected–rejected connectivity (top right). Scatter plots at the bottom show linear regressions (with 95% confidence bands) of participant selection contrast for rITG–rFFA connectivity on continuous age for non-anxious (bottom left) and anxious (bottom right) participants.
connectivity between the rFFA and lACC was significantly correlated with the memory bias. Specifically, higher rFFA–lACC connectivity when receiving positive versus negative peer feedback was associated with greater memory bias for positive versus negative peer feedback (Fig. 6). There were no group differences in this association.

Figure 5  The left pregenual anterior cingulate cortex (lACC) exhibited a significant age group by diagnosis interaction for the peer feedback contrast (overlaid on structural images at left). Graphs at the top show mean (± SEM) right fusiform face area (rFFA) connectivity during positive and negative peer feedback (top left) and mean (± SEM) contrast of positive–negative connectivity (top right). Scatter plots at the bottom show linear regressions (with 95% confidence bands) of peer feedback contrast for lACC–rFFA connectivity on continuous age for non-anxious (bottom left) and anxious (bottom right) participants.

Figure 6  The box plot (left) displays distributions of memory bias for peer feedback recall in the four participant groups. Positive values indicate greater memory for positive peer feedback, and negative values indicate greater memory for negative peer feedback. The scatter plot (right) depicts the association between memory bias (on the y-axis) and lACC–rFFA coupling (on the x-axis) (with 95% confidence bands).
DISCUSSION

We identified several group differences in functional rFFA connectivity that related to participants’ selection or rejection of peers for a future online chat and the valence of feedback associated with those peers’ faces. In particular, anxious and non-anxious participants showed different patterns of rFFA connectivity when viewing faces of peers they had previously selected versus rejected in areas of visual cortex and cerebellum. Developmental differences in rFFA connectivity patterns across anxiety groups emerged in the right anterior temporal gyrus and left cerebellum as a function of participant selection, and in the left pregenual anterior cingulate cortex as a function of peer feedback. Finally, we found evidence of an association across all participants between rFFA–lACC co-activation and subsequent memory bias. We will consider each of these findings in turn.

Among anxious participants, three regions in the occipital lobe (left lingual gyrus/cuneus, bilateral regions of fusiform) were more strongly coupled to the rFFA when viewing faces of peers they had rejected than ones they had selected on the initial visit, while non-anxious participants demonstrated the opposite pattern (Fig. 3). These regions have previously been characterised as part of the face processing network (Haxby, Hoffman, & Gobbini, 2002; Weiner & Grill-Spector, 2012), acting as components of the ventral visual stream to support perception. Co-activation suggests that socially anxious individuals dedicate more resources to processing faces they had rejected than those they had selected, consistent with other findings from this task concerning the salience of rejected peers (Guyer et al., 2008; Spielberg et al., 2015), and may reflect greater neural processing of potentially negative than potentially positive outcomes among anxious individuals. This interpretation is speculative, however, and awaits further study.

We observed a similar anxiety-based shift in co-activation within the rITG (Fig. 4), although this difference interacted with age. Post hoc comparisons confirmed that anxious juveniles uniquely showed greater connectivity when receiving feedback from peers they had previously rejected. The rITG is also part of the ventral visual stream, although this region is much further downstream from the occipital regions noted above. As visual percepts advance along the visual stream, they become increasingly integrated with other information. In the inferior temporal cortex, social stimuli may be particularly sensitive to valence modulations (Hadj-Bouziane et al., 2012; Morin, Hadj-Bouziane, Stokes, Ungerleider, & Bell, 2014). Therefore, the finding that anxious juveniles co-activate this region more when viewing previously rejected, relative to selected, faces may reflect the same framing bias that was driving the activation in the occipital lobe, but possibly more closely tied to affect than attention. If so, this appears to be a feature of social anxiety that is particularly marked in younger individuals and diminishes across maturation, possibly reflecting the greater affective potency of peer acceptance for adolescents than adults.

A final age by diagnosis effect was found in a large cluster in the pregenual ACC (Fig. 5). In contrast to other findings, where connectivity differences related to participant selection or rejection of peers, these findings related to the valence of peer feedback. Here, we found that in anxious juveniles, left pregenual ACC–rFFA coupling was stronger following negative than positive peer feedback, whereas this coupling was reversed for the other three groups. Thus, as with the findings with the rITG, the anxious juveniles appear to have a unique pattern of rFFA–lACC coupling. Several functions that have been attributed to the IACC may relate to this task. These include mentalising, error monitoring, self-appraisal, and affect regulation (Melcher, Falkai, & Gruber, 2008; Rushworth, Mars, & Sallet, 2013; Sturm et al., 2013; Tang, Posner, Rothbart, & Volkow, 2015). This region also has strong associations with internalising disorders (Murray, Wise, & Drevets, 2011). Although it is difficult to say which psychological processes were engaged in anxious juveniles relative to other groups, it is clear that rFFA connectivity associated with faces in this task was biased towards negative rather than positive social information. These findings suggest that in contrast to all other groups, anxious juveniles devote greater neuronal resources to processing social information (e.g., regulating affect, monitoring own errors, mentalising) following a negative occurrence. This pattern unexpectedly reversed in anxious adults. This reversal may reflect a shift in the potency of peer rejection as anxious individuals shift into adulthood, a transition associated with psychopathology progression, or may be related to other non-specific aspects of this task. These results hint at compelling hypotheses related to the interaction of anxiety with development, which remain to be flushed out in future studies.

We should note that two different analyses of these same data or a subset of this data also found aberrant activity in the anxious juvenile group in regions similar to or even overlapping with the pregenual ACC. We have associated these findings with differences in prediction error processing (Jarcho et al., 2015) and anticipatory anxiety responses (Spielberg et al., 2015) in anxious juveniles. While these different models have generated slightly different interpretations of the role the ACC/medial PFC is playing in the integration of social information, in this sample, anxious juveniles are evidently engaging this region in a unique manner.

Finally, we found a significant relationship between rFFA–lACC connectivity and memory bias. Greater positive rFFA–lACC coupling during positive social feedback was associated with greater memory bias for positive feedback.
Although this relationship did not differ across groups, when considered together with the finding that anxious participants exhibited a bias towards expectation and recall of negative social feedback, this suggests that functional coupling between rFFA and pregenual ACC may relate to negative information bias that is a common cognitive feature of SAD (Coles & Heimberg, 2002; Foa, Gilboa-Schechtman, Amir, & Freshman, 2000; Lundh & Öst, 1996; Morrison & Heimberg, 2013; Roth & Heimberg, 2001).

One surprising outcome of this study is that we failed to see group differences in functional connectivity between rFFA and the amygdala or striatum. Hyperactivity within the amygdala in response to fearful or threatening face presentation is one of the more consistent findings in anxiety (Gentili et al., 2015), and as noted in the introduction, we have observed alterations in both the amygdala and striatum in this task previously (Guyer et al., 2008, 2014; Jarcho et al., 2015; Spielberg et al., 2015). Therefore, we expected to see a differential pattern of connectivity with the rFFA in this analysis. However, many of these effects are stronger during the anticipatory period, which precedes receipt of the response itself (Lau et al., 2011), and was not considered in this study.

**Limitations**

There are several important limitations in the interpretations of this study. First, although we have found significant age and diagnosis differences in functional coupling with the rFFA, without further corroborating data, we can only speculate on the clinical significance of brain differences. Clinically meaningful correlates such as self-reports or behavioural measures are clearly needed. Second, as with all developmental studies, cross-sectional measures are subject to a variety of confounding effects and, as such, are not as reliable as longitudinal measures to track maturational changes. Third, there are clear limitations of the categorical approach we adopted here for both age and diagnostic measures—particularly as not all of our patients met full criteria for SAD. While a categorical approach offered straightforward analyses and interpretations in terms of four distinct groups, use of continuous measures would enable a more detailed analysis of the variability in the data. Finally, the use of two scanners for data collection may have introduced artefacts between subjects. We used scanner as a covariate to help mitigate the potential impact of this on our analyses, although this may have reduced our power to detect differential functional coupling due to different scanner distributions across groups. In spite of these notable limitations, we feel that this study uncovered some important neuronal differences as a function of both anxiety status and age that warrant follow-up and replication in future studies.

**CONCLUSIONS**

In sum, our results were largely consistent with our predictions that co-activation with a face-responsive brain region in socially anxious and healthy individuals varied in a task-dependent manner. Results from healthy individuals suggest that greater neuronal resources are dedicated to perceptual processing of outcomes from potentially positive social interactions (peers previously selected by participants), whereas anxious individuals dedicate more resources to processing potentially negative interactions (peers previously rejected by participants). In some regions, this pattern was evident across development, whereas in others, it was primarily evident in the juvenile group. We attribute these brain differences to differential engagement of attention and/or emotion in anxiety, and they are likely a neuronal reflection of well-known cognitive biases in social anxiety.

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**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

**Table S1.** Statistically significant regions showing functional connectivity with the right fusiform face area during feedback in the Chatroom Task. Threshold of voxelwise $p \leq .005$ and minimum cluster size of 50 voxels. Coordinates are for maximum $t$-value.

**Table S2.** Anxiety diagnosis $\times$ participant selection interaction effect on right fusiform face area connectivity; analysis of data extracted from significant regions.

**Table S3.** Anxiety diagnosis $\times$ age group $\times$ participant selection interaction effect on right inferior temporal gyrus (rITG)–right fusiform face area (rFFA) connectivity; analysis of data extracted from significant region.

**Table S4.** Anxiety diagnosis $\times$ age group $\times$ peer feedback interaction effect on left anterior cingulate cortex (IACC)–right fusiform face area (rFFA) connectivity; analysis of data extracted from significant region.

**REFERENCES**


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