Positive valence bias is associated with inverse frontoamygdalar connectivity and less depressive symptoms in developmentally mature children

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Research Highlights

- A more negative valence bias was associated with depression symptoms for children in later stages of puberty.
- For children in later stages of puberty, more inverse mPFC-amygdala connectivity was associated with a more positive valence bias.
- A negative valence bias may be a healthy part of emotional functioning at early developmental stages, but maintaining this negativity is associated with dysfunction.
- Development of frontoamygdala connections may be critical for the development of healthy emotional functioning

Abstract

Negativity bias is a core feature of depression and anxiety that is associated with dysfunctional frontoamygdalar connectivity, a pathway associated with emotion regulation. We used a valence bias task (ratings of emotional ambiguity) as a potential early indicator of depression risk and differences in frontoamygdalar connectivity. Previous work using this task has demonstrated that children have a more negative bias than adolescents/adults. We propose that this negativity bias in childhood is normative, but its persistence in adulthood may result from differences in the development of emotion regulation mechanisms, and may be associated with increased depressive symptoms. In this limited age range (6-13 years), we tested the moderating role of puberty on relationships between valence bias, depressive symptoms, and frontoamygdalar connectivity. Only in later puberty, a negative bias was associated with increased depressive symptoms and more positive (immature) frontoamygdalar connectivity, whereas a more positive bias was associated with more inverse (adult-like) connectivity suggestive of emotion regulation. These data suggest that with maturation, individual differences in emotion regulation circuitry support a positive valence bias and possibly a reduced risk for depression. Longitudinal work is necessary to determine the directionality of these effects and explore the influence of early life events.

1.Introduction

Negativity bias is an enhanced attention to and memory for negatively valenced information (Browning, Holmes, & Harmer, 2010; Roy et al., 2008; Vasey, Daleiden, Williams, & Brown, 1995), and is thought to underpin the development and persistence of mood and anxiety conditions (Beck, 1976; Williams et al., 2007). In adults, this bias is stable (Neta, Norris, & Whalen, 2009; Williams et al., 2009) but can be overridden with emotion regulation strategies (Charles & Carstensen, 2007). However, the developmental origins of negativity bias remain poorly understood. Studies have shown that specific facial expressions can be useful elicitors of negativity bias. Although some expressions (e.g., happy or angry) signal clear valence information about the emotions and intentions of others, other expressions (e.g., surprise) are ambiguous because they signal both positive (e.g., winning the lottery) and negative events (e.g., witnessing an accident). When presented without contextual information, these ambiguous expressions are used to identify a *valence bias*, or one's tendency to interpret ambiguity as having a positive or negative meaning, and this bias is stable over time (Kim, Somerville, Johnstone, Alexander, & Whalen, 2003; Neta, Kelley, & Whalen, 2013; Neta et al., 2009).

In concert with profound developmental changes in emotional behavior that support functional social behavior (Denham, 1998; Eisenberg et al., 1993; John & Gross, 2004; Saarni, 1984) and predict mental health outcomes (Reef, Diamantopoulou, Meurs, Verhulst, & Ende, 2011), children relative to adults show a stronger negativity bias (Vaish, Grossmann, & Woodward, 2008). Accompanying these behavioral changes, there are neurobiological and structural brain changes during puberty (Blakemore, Burnett, & Dahl, 2010), such as decreased amygdala reactivity (Guyer et al., 2008; Hare et al., 2008; Monk et al., 2003; Swartz, Carrasco, Wiggins, Thomason, & Monk, 2014), and more inverse frontoamygdalar connectivity (Gabard-

Durnam et al., 2014; Gee, Humphreys, et al., 2013; Perlman & Pelphrey, 2011). The results from multiple studies suggest that this pattern of frontoamygdalar connectivity reflects an emotion regulatory process (Hare et al., 2008; Kim, Somerville, Johnstone, Alexander, & Whalen, 2003; Swartz, Carrasco, Wiggins, Thomason, & Monk, 2014), in which frontal regions downregulate amygdala activity during emotional processing (Hare et al., 2008; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; Pezawas et al., 2005). In addition, dysfunction of this pathway is associated with emotion-related disorders (Das et al., 2007; Gee, Gabard-Durnam, et al., 2013; Wang et al., 2009), which highlights its role in emotional control (Banks, Eddy, Angstadt, Nathan, & Phan, 2007). These findings suggest that early risk factors for depression vis-à-vis negativity bias may include developmental differences in emotion regulation strategies and brain circuitry.

Extant literature on negativity bias, which includes subclinical symptomology (Pagliaccio, Luby, Luking, Belden, & Barch, 2014), tends to use stimuli that rely on developmentally advanced cognitive/linguistic abilities. However, emotional valence conveyed through facial expressions is reliably identified in early childhood (Bruce et al., 2000; Widen & Russell, 2008), and can usefully probe negativity bias. Ambiguous (i.e., surprised) expressions in particular have been used to demonstrate a more negative valence bias in children (Tottenham, Phuong, Flannery, Gabard-Durnam, & Goff, 2013), consistent with the notion that a positive bias is supported by emotion regulation mechanisms. Given this sensitive period sees a shift in both valence bias and regulatory brain mechanisms, these developmental changes may pave the way toward a more healthy (or aberrant) emotion processing represented by a more positive (or negative) valence bias in adulthood. In other words, valence bias may be linked to developmental differences in emotion regulation brain circuitry, which may help identify early mental health risk factors. Using a cross-sectional design, we investigated the relationships between valence

bias, depressive symptoms, and emotion regulation circuitry within an age range demonstrated to show a more negative valence bias (ages 6-13 years; Tottenham et al., 2013) and a developing regulatory circuitry (Gabard-Durnam et al., 2014; Gee, Humphreys, et al., 2013; Perlman & Pelphrey, 2011; Silvers et al., 2017). We examined functional brain connectivity while viewing facial expressions during magnetic resonance imaging (MRI). Recent evidence indicates that brain development may be more closely tied to pubertal status than age (Blakemore et al., 2010), especially within restricted, developmentally sensitive age ranges (Goddings, Heyes, Bird, Viner, & Blakemore, 2012). Also, given that age represents a different stage in maturation for males and females (Schuiling & Likis, 2016), pubertal status – as opposed to age – served as our proxy for maturity. We predict that with increasing maturation, a more negative valence bias and a more immature amygdala-medial prefrontal cortex (mPFC) connectivity pattern may pose an increased risk for depression.

2. Materials and Methods

2.1 Participants. We estimated a sample size based on previous work that examined developmental differences (as measured by a continuous variable representing age or puberty) in brain responses to face stimuli (N=45; Fowler, Miernicki, Rudolph, & Telzer, 2017) and N=41; Gee, Humphreys, et al., 2013). However, given expected data loss due to difficulty remaining motionless in the scanner (Fowler et al., 2017; Klapwijk et al., 2013) and task performance in previous work (Neta et al., 2009), we collected data from 61 participants (28 female; ages 6-13 years, mean(SD) age = 9.20(2.15)). All participants were Caucasian to control for any cross-race effects when rating Caucasian faces. Six participants did not complete the neuroimaging portion of the task. An additional fourteen participants were excluded for failing to accurately rate the clearly valenced angry (N=4) and happy (N=10) expressions on at least 60% of trials, an accuracy threshold used for adult participants (Brown, Raio, & Neta, 2017; Neta et al., 2013,

2009; Neta, Tong, & Henley, 2018; Neta & Tong, 2016). The exclusion criteria for accuracy is particularly important because, if participants are not accurately rating angry faces as negative and happy as positive, then it is difficult to discern the specific valence interpretations of emotional ambiguity (i.e., valence bias). The final sample consisted of 41 participants (23 female; ages 6-13 years, mean(SD) age = 9.46(2.12)), that did not differ in age from those excluded (t_{59} = 1.51; p = .14; range = 6-13; mean(SD) age = 8.60(2.06)). We assessed pubertal status using the Petersen Puberty Development Scale (Petersen, Crockett, Richards, & Boxer, 1988), which was calculated as described by Petersen and colleagues (range represented the full spectrum of possible scores = 1-2.8, mean(SD) = 1.67(.56)). This questionnaire was completed by the child with instruction from the experimenter and is comprised of questions related to observable changes in the body (e.g. growth of body hair, deepening of voice). This measure of pubertal status was positively related to age (t_{39} = 6.68, p < .001, R^2 = .54) and not significantly different between the genders (t_{39} = 0.40, p =.69). The average full-scale intelligence quotient of the sample was within normal range as assessed by the 2 subset Wechsler Abbreviated Scale of Intelligence (WASI; range = 88-142; mean(SD) = 114.18(14.53); Wechsler, 1999), and did not correlate with age (r_{39} = -.10, p = .56) or pubertal status (r_{39} = -.07, p = .68). Depressive symptoms were quantified using the major depression subscale of the Revised Child Anxiety and Depression Scale (RCADS; range = 0-12, mean(SD) = 2.20(2.40); Chorpita, Yim, Moffitt, Umemoto, & Francis, 2000) administered to the child's parent to maintain consistency across the sample given the young ages. This scale has been validated in ages as young as 3 years (Ebesutani, Tottenham, & Chorpita, 2015). However, because our age range (6-13 years) extends below the minimum of standardized T scores (grades 3-12), raw scores of the major depression subscale were used in the analyses, consistent with a recent study (Vantieghem et al., 2017). One participant reported a major depression score of 12 which, while the age of this participant (7

years) was below the range included in the T scores, was associated with a T score in the youngest standardized sample (3rd grade) of 74, exceeding the cut-off associated with clinical diagnoses (T = 70; Chorpita et al., 2000). However, the inclusion of this participant did not qualitatively effect the reported results (see sections 3.1.2 and 3.2.1). All protocols were approved by the University of Nebraska Committee for the Protection of Human Subjects. The participants and their parent/legal guardian were informed of all procedures prior to the child's participation, and a parent/legal guardian of each participant gave written informed consent prior to testing in accordance with the Declaration of Helsinki.

2.2 Procedure

2.2.1 Session 1: behavioral. All experimental stimuli were presented on E-Prime software (version 2.0.10; Psychology Software Tools, Pittsburgh, PA). In Session 1 (Figure 1), participants performed a task to assess their baseline valence bias in which they viewed positive (e.g., happy), negative (e.g., angry), and ambiguous (e.g., surprised) images on a black background. For each image, participants were asked to make a two-alternative, forced-choice decision (via keyboard press) as quickly and as accurately as possible, indicating whether each image "felt good or felt bad"; this language and stimuli have been in previous work within similar age groups (Kestenbaum, 1992; Tottenham et al., 2013). This included a set of 48 faces, 24 with an ambiguous valence (surprised expression), and 24 with a clear valence (12 angry and 12 happy expressions). Of the 48 faces, 34 discrete face identities were used (17 males, 17 females) posing angry, happy, and surprised expressions. Fourteen identities (seven females, ages 21-30 years) were taken from the NimStim Set of Facial Expressions (Tottenham et al., 2009) and 20 (10 female, age 20-30 years) from the Karolinska Directed Emotional Faces database (Goeleven, De Raedt, Leyman, & Verschuere, 2008). All identities were European/European American. In separate but alternating blocks, scenes from the International

Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997) were presented, consisting of 24 scenes with an ambiguous valence and 24 with a clear valence (12 negative and 12 positive). The purpose of rating scenes was outside the scope of the current report, and did not contribute to the valence bias score nor were they included in subsequent analyses. All blocks of stimuli included 24 images (12 ambiguous, 6 positive, and 6 negative) presented in a pseudorandom order (see Figure 1 for a depiction of tasks). Each stimulus was presented for 1500ms followed by a fixation cross for either 200 or 1900ms. We calculated the valence bias for each participant as the percentage of times that a participant indicated that a particular surprised face felt bad (e.g., a valence bias was 100% if that participant rated surprised faces as bad on all trials). Participants and parents then completed surveys (see above) and participants completed a mock scan (see below).

2.2.2 Session 2: MRI. Session 2 followed Session 1 by approximately 9 days (mean(SD) days = 9.34(6.69), range 1-46 days). Days between sessions was unrelated to the behavioral (see section 3.1.2) and neuroimaging results (see section 3.2.1). Participants viewed a new set of European/European American faces from the Umeå University Database of Facial Expressions (Samuelsson, Jarnvik, Henningsson, Andersson, & Carlbring, 2012) across 4 experimental runs while positioned in a MRI scanner (Figure 1). Prior to entering the MRI, all participants underwent a mock scanning session to acclimate to the environment and practice instructions to remain still during scanning. Padding was used to secure the participants' head in a comfortable, static position. The experimenters provided feedback and reminders to remain still throughout the session.

Each experimental run consisted of 4 blocks of 12 face presentations. Faces were presented for 500 ms and separated by a fixed interstimulus interval of 1000 ms. The first 2 runs consisted of 2 blocks of surprised faces and 2 blocks of neutral faces, and the latter 2 runs

replaced surprised with fearful faces, all presented pseudo-randomly. An additional 3 pictures depicting flowers were pseudo-randomly presented during each block, to which the participants were instructed to make a response. All stimuli during this session were 500 x 750 pixels with a black background.

2.3 MRI Parameters

2.3.1 MRI data acquisition parameters. The MRI data were collected at the University of Nebraska-Lincoln, Center for Brain, Biology, & Behavior, on a Siemens 3T Skyra scanner using a 32-channel head coil. Structural images were acquired using a T1-weighted MPRAGE sequence (TR = 2.20 s, TE = 3.37 ms, slices = 192 interleaved, voxel size = 1.0 × 1.0 × 1.0 mm matrix = 256 × 256, FOV = 256 mm, flip angle = 7°, total acquisition time = 5:07). Blood oxygen level-dependent (BOLD) activity was measured using an EPI scanning sequence (TR = 2.50 s, TE = 30 ms, slides = 42 interleaved, voxel size = 2.50 × 2.50 × 2.80 mm, matrix = 88 × 88 mm, FOV = 220 mm, flip angle = 80°, total acquisition time = 3:14 per block) in which slices were acquired parallel to the intercommissural plane and the volume positioned to cover the extent of the entire brain.

2.3.2 Preprocessing. Preprocessing of MR images was conducted using the Analysis of Functional Neuroimages (AFNI) program suite (Cox, 1996). The first four TRs of each run were excluded to allow for scanner stabilization. Voxel time-series were first despiked by removing values with outlying data in each voxel's time-series separately. Then, slice timing correction was accomplished by re-referencing each scan to the first slice. These slice time corrected volumes were realigned to the minimum outlier image. Each volume was then aligned to the anatomical image before being warped to the Talairach template atlas (Talairach & Tournoux, 1988) provided by AFNI. Functional volumes were then spatially smoothed using a $6mm^3$ fwhm kernel. The BOLD time-series in each voxel separately was normalized by dividing each time

point by its average across all time points and then multiplying each time point by 100. Any images containing movements > .9mm^3, as determined by the motion parameters calculated during spatial realignment, were censored from further analysis. No participants showed excessive movements in more than 18% of their scans (Gee, Humphreys, et al., 2013), and no more than 6% during the presentation of any face expression. The number of censored scans did not differ between surprise and neutral trials (t_{40} = .74, p = .46), and was not correlated with participant age (r_{39} = -.18, p = .25).

2.4 Experimental Design and Statistical Analysis

2.4.1 Behavioral data analysis

See Table 1 for descriptive information of analyzed behavioral variables. Although the current study aimed to describe a puberty-moderated link between valence bias and both depressive symptoms and amygdala-mPFC connectivity, the cross-sectional design limited the possibility of inferring directional associations between these variables (e.g., valence bias impacts depressive symptoms or depressive symptoms impacts valence bias). We conducted two separate moderation analyses, first within the behavioral data, and second related to the MRI data (see section 2.4.4).

Because depressive symptoms were non-normally distributed (Shapiro-Wilk: W = .78, p = .00001), robust regression was used for the following analyses of the behavioral data. First, to determine whether a more negative valence bias was related to higher depressive symptoms, the two measures were submitted to a robust bivariate regression (calculated using the *fitlm* command in Matlab) in which valence bias was a predictor of depression. Then, the moderating effect of pubertal status on the relationship between valence bias and depressive symptoms was tested in a robust regression with valence bias as the outcome variable; this model had a constant term and four predictors: 1) depressive symptoms, 2) pubertal status, 3) the interaction between

depressive symptoms × pubertal status, and 4) age, which was included as a covariate. The interaction term coefficient represented the moderation effect.

2.4.2 BOLD reactivity. To identify brain regions in which BOLD activity related to each stimulus condition, the BOLD data were submitted to a general linear model (GLM) in which surprise, fear, and neutral blocks were modeled separately for the 4 runs of the experiment. These regressors included a boxcar function modeling the onset and duration of each block that was convolved with the hemodynamic response function. Each run included a constant term and nuisance regressors: 6 motion parameters (three rotational and three translational vectors) calculated during realignment, and both a linear and cubic polynomial trend model, consistent with AFNI guidelines given each runs' 172.5 s duration.

2.4.3 BOLD context-dependent connectivity. To assess the functional connectivity between the amygdala and the rest of the brain specific to each condition, a context-dependent connectivity analysis was conducted using AFNI commands. The seed amygdala region was defined as the voxels showing activation while viewing surprised expressions compared to baseline (the fixation period between blocks), exceeding a corrected threshold (FWE: $p < .05$) based on Gaussian Random Field theory (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994; Hayasaka & Nichols, 2003) that avoids the spatial autocorrelation issue raised by Eklund and colleagues (Eklund, Nichols, & Knutsson, 2016). This threshold consisted of both a cluster-forming ($p < 0.001$) and cluster-extent ($k > 21$) threshold. One voxel cluster showed peak activation in the right basal forebrain (peak-$t_{40} = 7.01$, $k = 86$; x = 17, y = -4, z = -11) and extended into the dorsal amygdala (Figure 3A), consistent with previous work demonstrating that the dorsal amygdala/substantia innominata is implicated in response to ambiguity (Kim, Somerville, McLean, et al., 2003; Whalen et al., 2009). The BOLD activity from this dorsal amygdala region was multiplied with boxcar functions modeling stimulus onsets and durations

separately for each condition, resulting in 4 condition-specific models of amygdala activity. These regressors entered a GLM with a constant term, task onset regressors, and a model of the amygdala activity across the whole duration of the experiment. Nuisance regressors consisted of the 6 motion models and, because the BOLD activity was analyzed across all runs continuously (690 seconds), 5 polynomial trends, consistent with AFNI guidelines.

2.4.4 mPFC-amygdala BOLD connectivity and valence bias. Connectivity between the amygdala and mPFC during emotional processing changes across development, such that there is a shift toward more inverse connectivity around age 10 years, thought to support age-related changes in emotion regulatory behaviors (Gee, Humphreys, et al., 2013). The amygdala seed region used in the current connectivity analysis was defined as voxels showing significant activation for surprise relative to baseline, a criterion chosen in order to include as many voxels sensitive to the surprised face expressions as possible. For comparison with valence bias and pubertal status, the connectivity beta differences for surprise *relative to neutral* were used in order to isolate amygdala connectivity specific to the ambiguity conveyed through the surprised expressions rather than a general response to facial expressions. To account for potential outlying data within any given voxel, robust regression was used for comparison with behavioral data. Thus, these surprise > neutral connectivity beta differences for each participant were submitted to a robust multiple regression (calculated using the *fitlm* command in Matlab) with a constant term and four predictors: 1) valence bias , 2) pubertal status, 3) the interaction between valence bias × pubertal status, and 4) age, which was included as a covariate. To determine whether pubertal status moderated the relationship between valence bias and amygdala connectivity in any mPFC region, the interaction term coefficient computed at each voxel separately, were passed through a cluster-forming ($p<0.01$) and -extent threshold ($k>75$) according to Guassian

Random Field theory guidelines for multiple comparison correction (Friston et al., 1994; Hayasaka & Nichols, 2003).

3. Results

3.1 Behavioral

3.1.1 Valence ratings – characterizing valence bias. Participants rated angry faces as negative (mean(SD) % negative = 85.91(11.75); range = 62-100), and happy faces as positive (mean(SD) % negative = 10.18(9.10); range = 0-30). In contrast, ratings of surprised faces showed greater variability (mean(SD) % negative = 64.66(21.75); range = 14-100), and represented the valence bias for each individual, such that higher scores indicated a more negative bias. Within this restricted age range, valence bias was not significantly correlated with age (r_{39} = -.12, p = .47) or pubertal status (r_{39} = -.06, p = .69).

3.1.2 Depressive symptoms and valence bias moderated by pubertal status. Table 1 lists the descriptive statistics for the behavioral variables. A bivariate robust regression revealed that valence bias was positively related to depressive symptoms (t_{39} = 2.29, p = .03, R^2 = .19), such that those with a more negative bias had higher depressive symptoms. For the moderation analysis, the interaction between depressive symptoms and pubertal status was significant (t_{36} = 2.48, p = .02; Figure 2) indicating that pubertal status, when controlling for age, moderated the relationship between depression and valence bias. To explore this moderation, the relationship between valence bias and depressive symptoms for each pubertal status was calculated. This relationship became significant between a pubertal status of 1.6-2.8 (out of possible scores of 1-2.8; Figure 2). To test for potential confounding effects, we ran similar moderation analyses that included gender or number of days between sessions 1 and 2 or excluded the participant with a supra-threshold clinical major depression score. Notably, the effects were qualitatively the same with each of these modifications, suggesting these variables did not impact the reported findings.

3.2 MRI

3.2.1 Context-dependent amygdala-mPFC connectivity and valence bias.

The relationship between surprise > neutral amygdala connectivity and valence bias, when controlling for age, was moderated by pubertal status in two clusters (Table 2). In other words, those with later pubertal status showed an effect whereby a more positive valence bias was associated with a more inverse (mature, i.e., suggestive of emotion regulation) connectivity in these regions. The first cluster showed peak activation in the right subcollosal gyrus (peak-t_{36} = 5.52, p = .000003; k=170; x = 11, y = -11, z = -14) and extended into the right rectal gyrus and right anterior cingulate. The second cluster showed peak activation in the left medial frontal gyrus (Figure 3B; peak-t_{36} = 4.50, p = .00007; k=92; x = -11, y = 49, z = -11) and extended into the left anterior cingulate, consistent with reports of amygdala connectivity with the mPFC (Kim, Somerville, Johnstone, et al., 2003). To explore the moderation within this latter mPFC cluster, the conditional effects of pubertal status were calculated from the intercept and slope of the relationship between valence bias and the voxel averaged amygdala-mPFC connectivity beta values; this was done at each level of pubertal status (min = 1, max = 2.8). These conditional effects (Figure 3C) indicated that for those with later pubertal status (status of 2 and up to the highest possible score of 2.8), the relationship between valence bias and amygdala-mPFC connectivity was more positive (Figure 3C, blue shaded area). In other words, more mature children with a less mature (positive) connectivity pattern had a more negative valence bias. In contrast, more mature children with a more mature (inverse) connectivity pattern had a more positive valence bias. The opposite effect (i.e., a more negative valence bias predicted more inverse amygdala-mPFC connectivity) was significant at a pubertal status starting at 1.6 down to the lowest possible score of 1 (Figure 3C, pink shaded area).

Finally, as with the behavioral results, we tested for potential confounding effects by rerunning the moderation analyses and including gender or number of days between sessions 1 and 2 or excluding the participant with a supra-threshold clinical major depression score. Notably, the effects were qualitatively the same with each of these modifications, suggesting these variables did not impact the reported findings.

4. Discussion

Emerging across puberty, a more negative valence bias was associated with more depressive symptoms and less inverse amygdala-mPFC connectivity (suggestive of weaker emotion regulation). These findings are consistent with our "initial negativity hypothesis" that posits that the initial or default interpretation of surprise is more negative (Neta, Davis, & Whalen, 2011; Neta & Tong, 2016; Neta & Whalen, 2010) and associated with increased amygdala activity (Kim, Somerville, Johnstone, et al., 2003; Neta & Whalen, 2010). In contrast, positive ratings depend upon slower and more elaborate emotion regulation processes which override the initial negativity and putatively downregulate the amygdala response (Kaffenberger, Brühl, Baumgartner, Jäncke, & Herwig, 2010; Kim, Somerville, Johnstone, et al., 2003; Neta et al., 2011; Neta & Tong, 2016; Neta & Whalen, 2010; Petro, Tong, Henley, & Neta, 2018), processes that are likely compromised in depression and anxiety (Beck, 1976; Reef et al., 2011; Williams et al., 2007). Indeed, age-related differences in this emotion regulation circuity (i.e., amygdala-mPFC connectivity (Gee, Humphreys, et al., 2013)) are associated with mental health risk factors in adults (Hare et al., 2008). The current results extend this "initial negativity hypothesis" by suggesting that individual differences in valence bias may originate during pubertal development, alongside the development of this emotion regulatory circuitry that putatively overrides the default, or initial negativity. Notably, these findings also support our model suggesting that the negative valence bias in early childhood is normative, but this negative

bias in later development is putatively *maintained* by the failure to develop a more mature, regulatory frontoamygdalar circuitry, which may *increase the risk* for depression.

Notably, while there was no explicit emotion regulation task, a more inverse frontoamygdala connectivity is thought to represent emotion regulation (Gee, Humphreys, et al., 2013; Ochsner et al., 2004). Indeed, the connectivity in these children spanned both positive and negative values, consistent with previous studies (Gee et al., 2013; Hare et al., 2008) which suggest that *inverse* connectivity (rather than a *lack of positivity connectivity*) may be associated with a more adult-like regulatory circuitry. While the current study treated connectivity as a continuous measure in order to test its relationship to valence bias and pubertal status, future work with larger sample sizes in normative adults should aim to identify the point at which negative frontoamygdalar connectivity defines an emotion regulatory process.

The utility of surprised faces in tracking individual differences in negativity bias and emotion regulation brain circuits is broadly consistent with a functional – contextual account of facial displays (Crivelli & Fridlund, 2018), which predicts that an expression's emotional value depends on its social, environmental, and/or cultural context (Barrett & Kensinger, 2010). Whereas happy and angry expressions signal predominantly positive or negative social outcomes, respectively, surprised faces signal multiple possible outcomes spanning positive and negative valence (i.e., dual valence ambiguity). Thus, the valence assigned to surprised expressions presented without context is more pliable to interpretation. The use of stimuli with dual valence ambiguity represents a methodological advance in conceptualizing negativity bias in that it side-steps limitations present in extant literature. For instance, negativity bias is often measured via either an attentional bias toward clearly negative *or* away from clearly positive stimuli (see Fales et al., 2008) or by examining responses to ambiguous stimuli with alternate meanings that could be either negative or neutral, but not positive (e.g. "lie"; Mathews et al.,

1989). These findings not only rely on cognitive/linguistic abilities not developmentally appropriate for children, but by not examining responses to stimuli with a dual-valence representation (i.e., negative *and* positive possible interpretations), these earlier findings are skewed toward the extremes of the valence spectrum. As such, this earlier work is limited in its ability to identify individual differences in responses to emotional stimuli during sensitive periods of development, and thus has more limited findings regarding the developmental origins of negativity bias. Future work will benefit from incorporating this task to examine individual differences in emotion reactivity and regulation, particularly in young ages.

These findings make a meaningful first step toward establishing the developmental origins of negativity bias. One caveat is the relatively small sample size with somewhat limited variance in depressive symptoms. Future work should replicate these findings in larger samples with a wider range of depressive symptoms and also determine the extent to which these findings, which use parent-reported subclinical depression (see; Muris, Meesters, & Fijen, 2003), generalize to those with clinically diagnosed or self-reported depression. Whether or not long-term mental health trajectories are impacted by environmental factors may also be explored. For instance, early life stress is a risk factor for mental health disorders (Tottenham et al., 2011) and is associated with developmental differences in regulatory circuitry (Heim & Binder, 2012; Lupien, McEwen, Gunnar, & Heim, 2009). The framework proposed here predicts that these developmental differences in brain function may produce a vulnerability to mental health disorders in the face of early life stress (Vantieghem et al., 2017), and is consistent with recent work showing that positive affect may serve as a buffer from the development of depressive symptoms (Sewart et al., 2019). Along these lines, frontoamygdalar differences may be linked to resiliency (Tugade & Fredrickson, 2004), the ability to find a positive outlook in potentially negative situations (Gross & John, 2003).

The moderating role of puberty on the relationship between valence bias and depressive symptoms occurred earlier in maturation (starting at a pubertal status of 1.6 and down to the lowest possible status of 1) than the relationship between valence bias and brain connectivity (starting at a pubertal status of 2 and up to the highest possible score of 2.8). Although cross-sectional, these findings provide preliminary evidence that a change toward a more positive valence bias and away from depressive symptoms has downstream effects on developing more adult-like brain connectivity patterns. Future longitudinal work is necessary to 1) test the prediction that the *maintenance* of negative valence bias is associated with both an increase in depressive symptoms and a slower development of amygdala-mPFC connectivity, and 2) establish the directionality these relationships. The opposite relationship between valence bias and amygdala-mPFC connectivity was also observed at a pubertal status of 1.4 and below. However, our predictions about the effects in early puberty were less clear, particularly before the point at which puberty moderates the link between valence bias and depressive symptoms (below a status of 1.6).

Because females and males show different age onsets in puberty (Schuiling & Likis, 2016), maturity was measured via pubertal development. In addition, followup analyses found gender was not related to pubertal moderation of amygdala-mPFC connectivity. Considering the age range of the current sample (6-13 years), these results are consistent with the finding that increased depression in females emerges *after* the age of 13 (Ferguson, Stegge, Miller, & Olsen, 1999; Hankin & Abramson, 2001). Continued work should explore whether gender differences emerge in older ages.

Future longitudinal work may also hold broad implications for treating mental health. For instance, the effects reported here may pinpoint developmental periods most sensitive to long-term mental health outcomes. Such information will be critical for informing potential

interventions (e.g., mindfulness), which can improve emotion regulation success and decrease negativity bias (Goldin & Gross, 2010; Jazaieri et al., 2014). These types of training may be particularly useful for individuals that putatively maintain a negativity bias beyond a normative developmental stage such that this bias interferes with normal, healthy functioning.

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Competing Interests

The authors declare that they have no competing interests.

Data Availabiltiy

The data relevant to this manuscript are available on the NIH National Database Archive.

References

Banks, S. J., Eddy, K. T., Angstadt, M., Nathan, P. J., & Phan, K. L. (2007). Amygdala–frontal connectivity during emotion regulation. *Social Cognitive and Affective Neuroscience*, *2*(4), 303–312. https://doi.org/10.1093/scan/nsm029

Barrett, L. F., & Kensinger, E. A. (2010). Context is routinely encoded during emotion perception. *Psychological Science*, *21*(4), 595–599. https://doi.org/10.1177/0956797610363547

Beck, A. T. (1976). *Cognitive therapy and the emotional disorders*. New York: International Universities Press.

Blakemore, S.-J., Burnett, S., & Dahl, R. E. (2010). The role of puberty in the developing adolescent brain. *Human Brain Mapping*, *31*(6), 926–933.

Brown, C. C., Raio, C. M., & Neta, M. (2017). Cortisol responses enhance negative valence perception for ambiguous facial expressions. *Scientific Reports*, *7*. https://doi.org/10.1038/s41598-017-14846-3

Browning, M., Holmes, E. A., & Harmer, C. J. (2010). The modification of attentional bias to emotional information: A review of the techniques, mechanisms, and relevance to emotional disorders. *Cognitive, Affective, & Behavioral Neuroscience*, *10*(1), 8–20. https://doi.org/10.3758/CABN.10.1.8

Bruce, V., Campbell, R. N., Doherty-Sneddon, G., Langton, S., McAuley, S., & Wright, R. (2000). Testing face processing skills in children. *British Journal of Developmental Psychology*, *18*(3), 319–333. https://doi.org/10.1348/026151000165715

Charles, S. T., & Carstensen, L. L. (2007). Emotion Regulation and Aging. In *Handbook of emotion regulation* (pp. 307–327). New York, NY, US: The Guilford Press.

Chorpita, B. F., Yim, L., Moffitt, C., Umemoto, L. A., & Francis, S. E. (2000). Assessment of symptoms of DSM-IV anxiety and depression in children: A revised child anxiety and depression scale. *Behaviour Research and Therapy*, *38*(8), 835–855.

Cox, R. W. (1996). AFNI: Software for Analysis and Visualization of Functional Magnetic Resonance Neuroimages. *Computers and Biomedical Research*, *29*(3), 162–173. https://doi.org/10.1006/cbmr.1996.0014

Crivelli, C., & Fridlund, A. J. (2018). Facial displays are tools for social influence. *Trends in Cognitive Sciences*, *22*(5), 388–399. https://doi.org/10.1016/j.tics.2018.02.006

Das, P., Kemp, A. H., Flynn, G., Harris, A. W. F., Liddell, B. J., Whitford, T. J., … Williams, L. M. (2007). Functional disconnections in the direct and indirect amygdala pathways for fear processing in schizophrenia. *Schizophrenia Research*, *90*(1), 284–294. https://doi.org/10.1016/j.schres.2006.11.023

Denham, S. A. (1998). *Emotional development in young children*. New York, NY, US: Guilford Press.

Ebesutani, C., Tottenham, N., & Chorpita, B. (2015). The revised child anxiety and depression scale - parent version: Extended applicability and validity for use with younger youth and children with histories of early-life caregiver neglect. *Journal of Psychopathology and Behavioral Assessment*, *37*(4), 705–718. https://doi.org/10.1007/s10862-015-9494-x

Eisenberg, N., Fabes, R. A., Bernzweig, J., Karbon, M., Poulin, R., & Hanish, L. (1993). The relations of emotionality and regulation to preschoolers' social skills and sociometric status. *Child Development*, *64*(5), 1418–1438.

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of*

Sciences of the United States of America, *113*(28), 7900–7905. https://doi.org/10.1073/pnas.1602413113

Fales, C. L., Barch, D. M., Rundle, M. M., Mintun, M. A., Snyder, A. Z., Cohen, J. D., … Sheline, Y. I. (2008). Altered emotional interference processing in affective and cognitive-control brain circuitry in major depression. *Biological Psychiatry*, *63*(4), 377–384. https://doi.org/10.1016/j.biopsych.2007.06.012

Ferguson, T. J., Stegge, H., Miller, E. R., & Olsen, M. E. (1999). Guilt, shame, and symptoms in children. *Developmental Psychology*, *35*(2), 347–357. https://doi.org/10.1037/0012-1649.35.2.347

Fowler, C. H., Miernicki, M. E., Rudolph, K. D., & Telzer, E. H. (2017). Disrupted amygdala-prefrontal connectivity during emotion regulation links stress-reactive rumination and adolescent depressive symptoms. *Developmental Cognitive Neuroscience*, *27*, 99–106. https://doi.org/10.1016/j.dcn.2017.09.002

Friston, K. J., Worsley, K. J., Frackowiak, R. S., Mazziotta, J. C., & Evans, A. C. (1994). Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping*, *1*(3), 210–220. https://doi.org/10.1002/hbm.460010306

Gabard-Durnam, L. J., Flannery, J., Goff, B., Gee, D. G., Humphreys, K. L., Telzer, E., … Tottenham, N. (2014). The development of human amygdala functional connectivity at rest from 4 to 23years: A cross-sectional study. *NeuroImage*, *95*, 193–207. https://doi.org/10.1016/j.neuroimage.2014.03.038

Gee, D., Gabard-Durnam, L., Flannery, J., Goff, B., Humphreys, K., Telzer, E., … Tottenham, N. (2013). Early developmental emergence of human amygdala–prefrontal connectivity after maternal deprivation. *Proceedings of the National Academy of Sciences of the*

United States of America, *110*(39), 15638–15643. https://doi.org/10.1073/pnas.1307893110

Gee, D., Humphreys, K., Flannery, J., Goff, B., Telzer, E. H., Shapiro, M., … Tottenham, N. (2013). A developmental shift from positive to negative connectivity in human amygdala–prefrontal circuitry. *Journal of Neuroscience*, *33*(10), 4584–4593. https://doi.org/10.1523/JNEUROSCI.3446-12.2013

Goddings, A., Heyes, S. B., Bird, G., Viner, R. M., & Blakemore, S. J. (2012). The relationship between puberty and social emotion processing. *Developmental Science*, *15*(6), 801–811. https://doi.org/10.1111/j.1467-7687.2012.01174.x

Goeleven, E., De Raedt, R., Leyman, L., & Verschuere, B. (2008). The karolinska directed emotional faces: A validation study. *Cognition and Emotion*, *22*(6), 1094–1118. https://doi.org/10.1080/02699930701626582

Goldin, P. R., & Gross, J. J. (2010). Effects of mindfulness-based stress reduction (mbsr) on emotion regulation in social anxiety disorder. *Emotion*, *10*(1), 83–91. https://doi.org/10.1037/a0018441

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology*, *85*(2), 348–362. https://doi.org/10.1037/0022-3514.85.2.348

Guyer, A. E., Monk, C. S., McClure-Tone, E. B., Nelson, E. E., Roberson-Nay, R., Adler, A. D., … Ernst, M. (2008). A developmental examination of amygdala response to facial expressions. *Journal of Cognitive Neuroscience*, *20*(9), 1565–1582. https://doi.org/10.1162/jocn.2008.20114

Hankin, B. L., & Abramson, L. Y. (2001). Development of gender differences in depression: An elaborated cognitive vulnerability-transactional stress theory. *Psychological Bulletin*, *127*(6), 773–796.

Hare, T. A., Tottenham, N., Galvan, A., Voss, H. U., Glover, G. H., & Casey, B. J. (2008). Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. *Biological Psychiatry*, *63*(10), 927–934. https://doi.org/10.1016/j.biopsych.2008.03.015

Hariri, A. R., Mattay, V. S., Tessitore, A., Fera, F., & Weinberger, D. R. (2003). Neocortical modulation of the amygdala response to fearful stimuli. *Biological Psychiatry*, *53*(6), 494–501. https://doi.org/10.1016/S0006-3223(02)01786-9

Hayasaka, S., & Nichols, T. E. (2003). Validating cluster size inference: Random field and permutation methods. *NeuroImage*, *20*(4), 2343–2356.

Heim, C., & Binder, E. B. (2012). Current research trends in early life stress and depression: Review of human studies on sensitive periods, gene–environment interactions, and epigenetics. *Experimental Neurology*, *233*(1), 102–111. https://doi.org/10.1016/j.expneurol.2011.10.032

Jazaieri, H., McGonigal, K., Jinpa, T., Doty, J. R., Gross, J. J., & Goldin, P. R. (2014). A randomized controlled trial of compassion cultivation training: Effects on mindfulness, affect, and emotion regulation. *Motivation and Emotion*, *38*(1), 23–35. https://doi.org/10.1007/s11031-013-9368-z

John, O. P., & Gross, J. J. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *Journal of Personality*, *72*(6), 1301–1333. https://doi.org/10.1111/j.1467-6494.2004.00298.x

Kaffenberger, T., Brühl, A. B., Baumgartner, T., Jäncke, L., & Herwig, U. (2010). Negative bias of processing ambiguously cued emotional stimuli. *Neuroreport*, *21*(9), 601–605. https://doi.org/10.1097/WNR.0b013e328337ff18

Kestenbaum, R. (1992). Feeling happy versus feeling good: The processing of discrete and global categories of emotional expressions by children and adults. *Developmental Psychology*, *28*(6), 1132–1142. https://doi.org/10.1037/0012-1649.28.6.1132

Kim, H., Somerville, L. H., Johnstone, T., Alexander, A. L., & Whalen, P. J. (2003). Inverse amygdala and medial prefrontal cortex responses to surprised faces. *NeuroReport*, *14*(18), 2317.

Kim, H., Somerville, L. H., McLean, A. A., Johnstone, T., Shin, L. M., & Whalen, P. J. (2003). Functional mri responses of the human dorsal amygdala/substantia innominata region to facial expressions of emotion. *Annals of the New York Academy of Sciences*, *985*(1), 533–535. https://doi.org/10.1111/j.1749-6632.2003.tb07120.x

Klapwijk, E. T., Goddings, A.-L., Burnett Heyes, S., Bird, G., Viner, R. M., & Blakemore, S.-J. (2013). Increased functional connectivity with puberty in the mentalising network involved in social emotion processing. *Hormones and Behavior*, *64*(2), 314–322. https://doi.org/10.1016/j.yhbeh.2013.03.012

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International affective picture system (IAPS): Technical manual and affective ratings. *NIMH Center for the Study of Emotion and Attention*, 39–58.

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*(6), 434–445. https://doi.org/10.1038/nrn2639

Mathews, A., Richards, A., & Eysenck, M. (1989). Interpretation of homophones related to threat in anxiety states. *Journal of Abnormal Psychology*, *98*(1), 31–34.

Monk, C. S., McClure, E. B., Nelson, E. E., Zarahn, E., Bilder, R. M., Leibenluft, E., … Pine, D. S. (2003). Adolescent immaturity in attention-related brain engagement to emotional facial expressions. *NeuroImage*, *20*(1), 420–428. https://doi.org/10.1016/S1053-8119(03)00355-0

Muris, P., Meesters, C., & Fijen, P. (2003). The self-perception profile for children: Further evidence for its factor structure, reliability, and validity. *Personality and Individual Differences*, *35*(8), 1791–1802. https://doi.org/10.1016/S0191-8869(03)00004-7

Neta, M., Davis, F. C., & Whalen, P. J. (2011). Valence resolution of facial expressions using an emotional oddball task. *Emotion*, *11*(6), 1425–1433. https://doi.org/10.1037/a0022993

Neta, M., Kelley, W. M., & Whalen, P. J. (2013). Neural responses to ambiguity involve domain-general and domain-specific emotion processing systems. *Journal of Cognitive Neuroscience*, *25*(4), 547–557. https://doi.org/10.1162/jocn_a_00363

Neta, M., Norris, C. J., & Whalen, P. J. (2009). Corrugator Muscle Responses Are Associated With Individual Differences in Positivity-Negativity Bias. *Emotion*, *9*(5), 640–648. https://doi.org/10.1037/a0016819

Neta, M., & Tong, T. T. (2016). Don't like what you see? Give it time: Longer reaction times associated with increased positive affect. *Emotion*, *16*(5), 730–739. https://doi.org/10.1037/emo0000181

Neta, M., Tong, T. T., & Henley, D. J. (2018). It's a matter of time (perspectives): Shifting valence responses to emotional ambiguity. *Motivation and Emotion*, *42*(2), 258–266. https://doi.org/10.1007/s11031-018-9665-7

Neta, M., & Whalen, P. J. (2010). The Primacy of Negative Interpretations When Resolving the Valence of Ambiguous Facial Expressions. *Psychological Science*, *21*(7), 901–907. https://doi.org/10.1177/0956797610373934

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: Neural systems supporting the cognitive down-and up-regulation of negative emotion. *Neuroimage*, *23*(2), 483–499. https://doi.org/10.1016/j.neuroimage.2004.06.030

Pagliaccio, D., Luby, J. L., Luking, K. R., Belden, A. C., & Barch, D. M. (2014). Brain-behavior relationships in the experience and regulation of negative emotion in healthy children: Implications for risk for childhood depression. *Development and Psychopathology*, *26*(4), 1289–1303. https://doi.org/10.1017/S0954579414001035

Perlman, S. B., & Pelphrey, K. A. (2011). Developing connections for affective regulation: Age-related changes in emotional brain connectivity. *Journal of Experimental Child Psychology*, *108*(3), 607–620. https://doi.org/10.1016/j.jecp.2010.08.006

Petersen, A. C., Crockett, L., Richards, M., & Boxer, A. (1988). A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of Youth and Adolescence*, *17*(2), 117–133. https://doi.org/10.1007/BF01537962

Petro, N. M., Tong, T. T., Henley, D. J., & Neta, M. (2018). Individual differences in valence bias: FMRI evidence of the initial negativity hypothesis. *Social Cognitive and Affective Neuroscience*, *13*(7), 687–698. https://doi.org/10.1093/scan/nsy049

Pezawas, L., Meyer-Lindenberg, A., Drabant, E. M., Verchinski, B. A., Munoz, K. E., Kolachana, B. S., … Weinberger, D. R. (2005). 5-HTTLPR polymorphism impacts human cingulate-amygdala interactions: A genetic susceptibility mechanism for depression. *Nature Neuroscience*, *8*(6), 828–834. https://doi.org/10.1038/nn1463

Reef, J., Diamantopoulou, S., Meurs, I. van, Verhulst, F. C., & Ende, J. van der. (2011). Developmental trajectories of child to adolescent externalizing behavior and adult DSM-IV disorder: Results of a 24-year longitudinal study. *Social Psychiatry and Psychiatric Epidemiology*, *46*(12), 1233–1241. https://doi.org/10.1007/s00127-010-0297-9

Roy, A. K., Vasa, R. A., Bruck, M., Mogg, K., Bradley, B. P., Sweeney, M., … Pine, D. S. (2008). Attention bias toward threat in pediatric anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, *47*(10), 1189–1196. https://doi.org/10.1097/CHI.0b013e3181825ace

Saarni, C. (1984). An observational study of children's attempts to monitor their expressive behavior. *Child Development*, *55*(4), 1504–1513. https://doi.org/10.2307/1130020

Samuelsson, H., Jarnvik, K., Henningsson, H., Andersson, J., & Carlbring, P. (2012). The Umeå university database of facial expressions: A validation study. *Journal of Medical Internet Research*, *14*(5). https://doi.org/10.2196/jmir.2196

Schuiling, K. D., & Likis, F. E. (2016). *Women's Gynecologic Health*. Jones & Bartlett Learning.

Sewart, A. R., Zbozinek, T. D., Hammen, C., Zinbarg, R. E., Mineka, S., & Craske, M. G. (2019). Positive affect as a buffer between chronic stress and symptom severity of emotional disorders. *Clinical Psychological Science*. https://doi.org/10.1177/2167702619834576

Silvers, J. A., Insel, C., Powers, A., Franz, P., Helion, C., Martin, R. E., … Ochsner, K. N. (2017). VlPFC–vmPFC–Amygdala Interactions Underlie Age-Related Differences in Cognitive Regulation of Emotion. *Cerebral Cortex*, *27*(7), 3502–3514. https://doi.org/10.1093/cercor/bhw073

Swartz, J. R., Carrasco, M., Wiggins, J. L., Thomason, M. E., & Monk, C. S. (2014). Age-related changes in the structure and function of prefrontal cortex–amygdala circuitry in children and adolescents: A multi-modal imaging approach. *NeuroImage*, *86*, 212–220. https://doi.org/10.1016/j.neuroimage.2013.08.018

Talairach, P., & Tournoux, J. (1988). *Co-Planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System: An Approach to Cerebral Imaging*. New York: Thieme Medical.

Tottenham, N., Hare, T. A., Millner, A., Gilhooly, T., Zevin, J., & Casey, B. J. (2011). Elevated amygdala response to faces following early deprivation. *Developmental Science*, *14*(2), 190–204. https://doi.org/10.1111/j.1467-7687.2010.00971.x

Tottenham, Nim, Phuong, J., Flannery, J., Gabard-Durnam, L., & Goff, B. (2013). A negativity bias for ambiguous facial expression valence during childhood: Converging evidence from behavior and facial corrugator muscle responses. *Emotion*, *13*(1), 92–103. https://doi.org/10.1037/a0029431

Tottenham, Nim, Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., … Nelson, C. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242–249. https://doi.org/10.1016/j.psychres.2008.05.006

Tugade, M. M., & Fredrickson, B. L. (2004). Resilient individuals use positive emotions to bounce back from negative emotional experiences. *Journal of Personality and Social Psychology*, *86*(2), 320–333. https://doi.org/10.1037/0022-3514.86.2.320

Vaish, A., Grossmann, T., & Woodward, A. (2008). Not all emotions are created equal: The negativity bias in social-emotional development. *Psychological Bulletin*, *134*(3), 383–403. https://doi.org/10.1037/0033-2909.134.3.383

Vantieghem, M. R., Gabard-Durnam, L., Goff, B., Flannery, J., Humphreys, K. L., Telzer, E. H., … Tottenham, N. (2017). Positive valence bias and parent–child relationship security moderate the association between early institutional caregiving and internalizing symptoms. *Development and Psychopathology*, *29*(2), 519–533. https://doi.org/10.1017/S0954579417000153

Vasey, M. W., Daleiden, E. L., Williams, L. L., & Brown, L. M. (1995). Biased attention in childhood anxiety disorders: A preliminary study. *Journal of Abnormal Child Psychology*, *23*(2), 267–279. https://doi.org/10.1007/BF01447092

Wang, F., Kalmar, J. H., He, Y., Jackowski, M., Chepenik, L. G., Edmiston, E. E., … Blumberg, H. P. (2009). Functional and Structural Connectivity Between the Perigenual Anterior Cingulate and Amygdala in Bipolar Disorder. *Biological Psychiatry*, *66*(5), 516–521. https://doi.org/10.1016/j.biopsych.2009.03.023

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence*. San Antonio, TX: The Psychological Corporation.

Whalen, P.]., Davis, F. C., Oler, J. A., Kim, H., Kim, M. J., & Neta, M. (2009). Human amygdala responses to facial expressions of emotion. In *The human amygdala.* (pp. 265–288). New York, NY, US: Guilford Press.

Widen, S. C., & Russell, J. A. (2008). Children acquire emotion categories gradually. *Cognitive Development*, *23*(2), 291–312. https://doi.org/10.1016/j.cogdev.2008.01.002

Williams, L. M., Gatt, J. M., Schofield, P. R., Olivieri, G., Peduto, A., & Gordon, E. (2009). "Negativity bias" in risk for depression and anxiety: Brain–body fear circuitry correlates, 5-HTT-LPR and early life stress. *NeuroImage*, *47*(3), 804–814. https://doi.org/10.1016/j.neuroimage.2009.05.009

Williams, L. M., Kemp, A. H., Felmingham, K., Liddell, B. J. ., Palmer, D. M., & Bryant, R. A. (2007). Neural biases to convert and overt signals of fear: Dissociation by trait anxiety and depression. *Journal of Cognitive Neuroscience*, *19*(10), 1595–1608. https://doi.org/10.1162/jocn.2007.19.10.1595

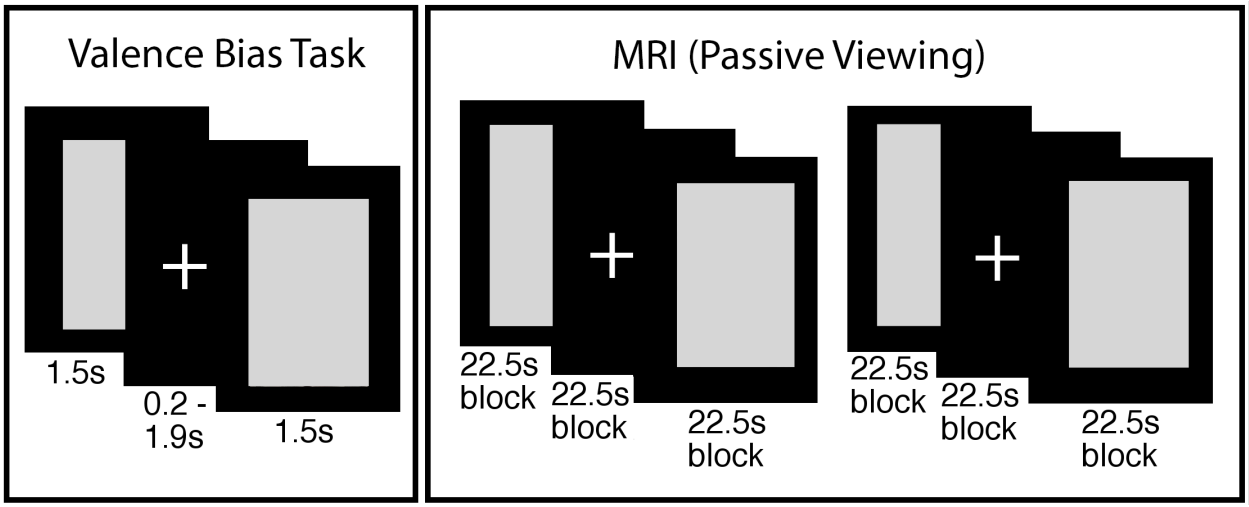

Figure 1. Depiction of Procedure. In this illustration, gray boxes replace face stimuli as per bioRxiv requirements. In the valence bias task, participants viewed happy, angry, and surprised faces, and indicated whether each image "felt good or felt bad." In the MRI, participants passively viewed new faces (i.e., not overlapping with the valence bias task) during two runs with blocks of surprised and neutral faces, and two runs with blocks of fearful and neutral faces.

Table 1. Descriptive statistics for behavioral variables.

Variables	Mean (SD)	Min	Max
Valence Bias (mean % negative)	64.66% (21.76%)	14.29%	100%
Depressive Symptoms (RCADS – Major Depression (Chorpita et al., 2000))	2.20 (2.40)	0	12
Pubertal status (Petersen Pubertal Development Scale (Petersen et al., 1988))	1.67 (.56)	1	2.8
Days Between Sessions	9.34 (6.69)	1	46

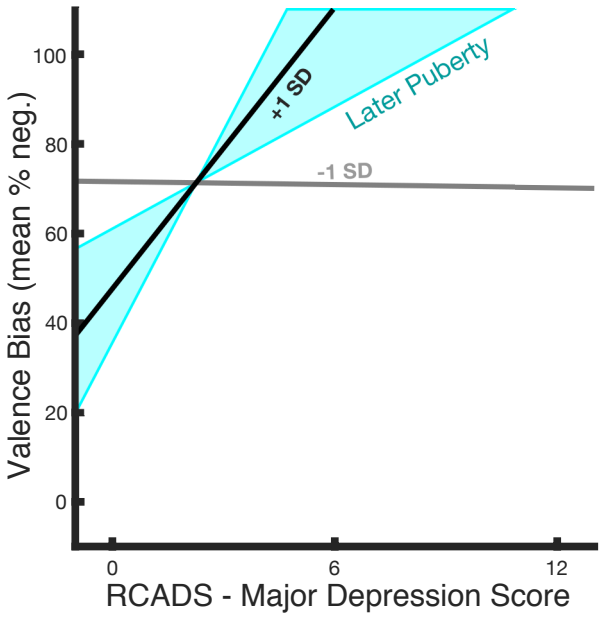

Figure 2. Relationship between valence bias and depressive symptoms. The relationship between depressive symptoms and valence bias was moderated by pubertal status ($t_{36} = 2.48$, $p = .02$) such that valence bias and depressive symptoms shared a stronger positive relationship at later pubertal stages. The estimated regression slopes for the relationship between valence bias and depressive symptoms at different pubertal stages illustrate that an earlier pubertal status (gray line; 1 standard deviation below the mean pubertal status; $t_{36} = -.06$, $p = .95$) predicted no relationship, whereas a later pubertal status (black line; 1 standard deviation above the mean pubertal status; $t_{36} = 2.63$, $p = .01$) predicted a positive relationship (blue shaded area denotes region of significance).

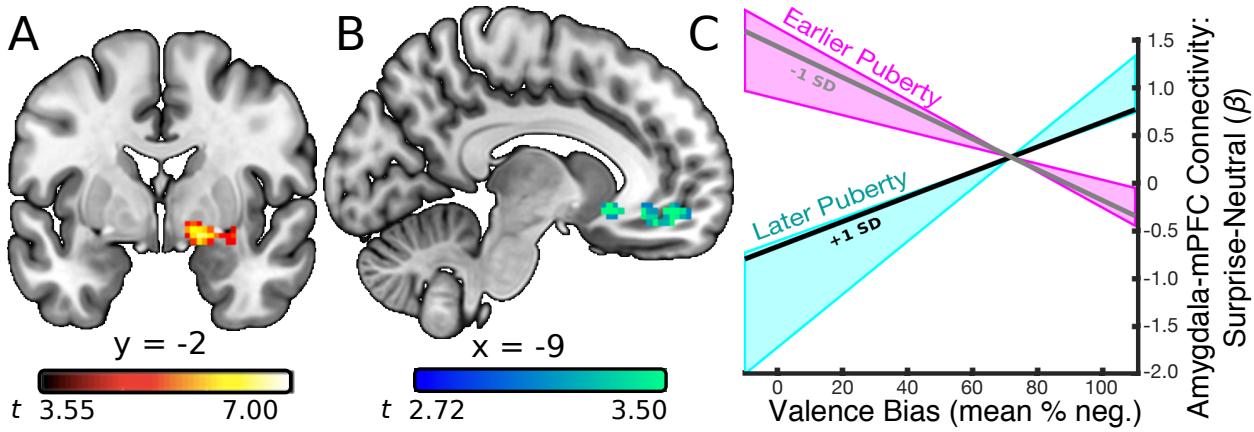

Figure 3. Relationship between amygdala-mPFC connectivity and negative valence bias as a function of pubertal status. A) A seed region in the right amygdala was defined using the contrast of surprised facial expressions versus baseline ($p < 0.0005$). **B)** The relationship between valence bias and amygdala connectivity was moderated by pubertal status in both the subcollasol gyrus (peak-$t_{36} = 5.52$, $p = .000003$) and the mPFC (peak-$t_{36} = 4.50$, $p = .00007$). **C)** The estimated regression slopes between valence bias and the surprise – neutral amygdala-mPFC connectivity betas, at an earlier (gray line; 1 standard deviation below the mean pubertal status; $t_{36} = -4.89$, $p = .00002$) and later (black line; 1 standard deviation above the mean pubertal status; $t_{36} = 3.52$, $p = .001$) pubertal status illustrates that more mature children (blue shaded area denotes region of significance) that have a mature (inverse) connectivity pattern were more likely to have a positive valence bias while those that have the less mature (positive) connectivity pattern were more likely to show a negative valence bias. Earlier pubertal status (pink shaded area denotes region of significance) predicted the *opposite* relationship between valence bias and amygdala-mPFC connectivity.

Table 2. Clusters of significant BOLD surprise > neutral amygdala connectivity: relationship with valence bias moderated by pubertal status

Region	**x**	**y**	**z**	**peak-t**	**k**
R Subcollosal Gyrus	11	-11	-14	5.52	170
L Medial Frontal Gyrus	-11	49	-11	4.50	92