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Multimodal examination of emotion processing systems associated with negative affectivity across early childhood

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ABSTRACT

High Temperamental Negative Affectivity in early childhood has been found to predict later emotion dysregulation. While much work has been conducted to separately probe bio-behavioral systems associated with Negative Affectivity, very little work has examined the relations among multiple systems across age. In this study, we use multi-modal methods to index neurobiological systems associated with Negative Affectivity in 53 4-7-year-old children. Prefrontal activation during emotion regulation was measured using functional near-infrared spectroscopy over the lateral prefrontal cortex (PFC) while children played a game designed to elicit frustration in Social (Happy and Angry faces) and Nonsocial contexts. Gaze behaviors while free-viewing Happy and Angry faces were also measured. Finally, Negative Affectivity was indexed using a score composite based on factor analysis of parent-reported temperament. Using mixed-effects linear models, we found an age-dependent association between Negative Affectivity and both PFC activation during frustration and fixation duration on the mouth area of Happy faces, such that older children high in Negative Affectivity spent less time looking at the mouths of Happy faces and had lower PFC activation in response to frustration (*ps*<0.034). These results provide further insight to how Negative Affectivity may be associated with changes in affective neurobiological systems across early childhood.

1. Introduction

Early childhood is marked by rapid maturation in emotional functioning, however the neurobiological basis of emotional development is not well understood. Temperament, defined as individual differences in emotional regulation and reactivity, is conceptualized to be relatively stable across individuals (Rothbart, 2007). Previous work has found that early childhood temperament—specifically the Negative Affectivity domain, which includes fearful, angry/frustrated, and sad behaviors—is a consistent predictor of later emotional functioning, including internalizing psychopathology (Karevold et al., 2012; Nigg, 2006; Rothbart et al., 2011). Negative Affectivity includes both automatic and deliberate emotion processing behaviors (e.g., orienting to threat or deliberate self-regulation), which are governed by numerous coordinated bio-behavioral systems (Lemerise and Arsenio, 2000). Careful characterization of these bio-behavioral systems may provide insight into early temperamental risk. For example, attentional biases for affective content are associated with internalizing psychopathology (Bar-Haim et al., 2007; Keil et al., 2018; Perez-Edgar et al., 2010)(, and there is emerging evidence for a neurodevelopmental origin to these attentional tendencies that may influences risk for these disorders (for a review, see Morales et al., 2016). While there have been many studies of associations between temperament and singular bio-behavioral systems, very few have examined multiple systems in the same sample of children. Considering the dramatic improvements in both emotion regulation and emotional processing across early childhood, examining the coordinated shifts in foundational systems across this age is of particular importance. Multimodal characterization of biological systems associated with Negative Affectivity across early childhood could provide important insight to how individual differences in these systems confer long-term emotional dysregulation.

There is evidence that individual differences in processing emotional information are associated with components of childhood Negative Affectivity, with much of this work examining attentional behavior in children with varying levels of fearful behaviors (behavioral inhibition, anxiety, or shyness). Attentional behavior both gates the initial stages of

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the emotional experience (orienting and encoding the pertinent aspects of environmental stimuli) and interacts with medial prefrontal components of emotion regulation systems in mutual exchange to influence later stages of emotional processing (Lemerise and Arsenio, 2000). Recent studies have found that five-to-seven-year-old children with higher fearful behaviors had a bias toward negative faces, though this bias was not stable within children longitudinally(Fu et al., 2019a,b; White et al., 2017). Another study of three-to-four-year-old children found no differences between clinically anxious children and typically-developing children in attentional patterns toward angry or neutral faces, though clinically anxious children spent less time gazing at the faces overall (Dodd et al., 2015). Together, these findings suggest that the association between fear and attentional bias towards negative faces may be an inverted-U-shape, with the dip towards avoidance occurring at clinically-impairing levels. In the only study, to our knowledge, to examine specific gaze behaviors during facial processing associated with temperamental variation, Matsuda et al. (2013) found that seven-to-thirteen-month-old infants high in fearful behaviors preferentially fixated on the eyes of strangers rather than the mouth. This work suggests that Negative Affectivity may be associated with individual differences in attentional patterns, however, how specific attentional patterns (e.g., fixating on the eyes versus the mouths of affective faces) shift across age is not clear. Across early childhood, there is evidence for rapid changes in emotion processing, such that children develop the ability to reliably identify affective content across this age (Boyatzis et al., 1993; Camras and Allison, 1985; Chronaki et al., 2015; Durand et al., 2007; Gao and Maurer, 2010). This suggests that there may be differences in attentional patterns across this period as children develop the skills to rapidly identify, and respond appropriately, to various affective circumstances.

There has been emerging evidence that individual differences in the neurobiological systems underlying emotion regulation are associated with individual differences in Negative Affectivity. Emotion regulation systems govern short- and long-term responses to external stimuli (Lemerise and Arsenio, 2000). These processes are thought to be largely coordinated by cortical regions that are together known as the fronto-parietal network (FPN), including regions of the dorsolateral prefrontal cortex (DLPFC) and intraparietal sulcus (Marek and Dosenbach, 2018). Importantly, there is evidence for marked improvements in emotional regulation across the early childhood period (Montroy et al., 2016), suggesting a development of the FPN alongside the emergence of increasingly sophisticated emotion regulation skills. The recent adoption of functional Near Infrared Spectroscopy (fNIRS) has enabled researchers to study FPN activation in young children by allowing for movement during testing. Recent work in children has found that, in normative samples, increased prefrontal activation was associated with increased Negative Affectivity while the opposite has been found in clinically dysregulated children (Grabell et al., 2018; Perlman et al., 2015, 2014). As of yet, very little work has been done to examine how this association may shift across age. Given that children develop their emotion regulation skills with caregiver scaffolding (Calkins, 2007; Fox and Calkins, 2003), it is likely that the association between Negative Affectivity and emotion regulation skills shifts with age, such that as children get older there are fewer instances of negative emotion elicitation and improvements in self-regulation.

The present study aims to use a multi-modal approach to characterize the bio-behavioral systems that comprise temperamental Negative Affectivity across early childhood. Specifically, we indexed emotional regulation in four-to-seven-year-old children using a novel frustration paradigm while imaging the PFC using fNIRS. We indexed attentional patterns using a free-viewing picture task and measured gaze dwell time on the eyes or mouth regions of Happy and Angry faces. Each of these metrics was then examined in the context of parent-reported temperamental Negative Affectivity. We hypothesized that children higher in Negative Affectivity would display greater PFC activation during frustration and that this effect would be larger in older, more developed children. We also predicted that children high in Negative Affectivity would spend more time gazing at the eyes and mouths of Angry faces and less time looking at these features in Happy faces.

2. Methods

2.1. Study procedures

All study procedures were approved by the Institutional Review Board at the University of Pittsburgh. Written consent and verbal assent were obtained from parents and children respectively. Four-to-seven-year-old children and their parents were recruited from the Pittsburgh area through paper and digital advertisements. Families were invited to the laboratory to complete in-lab questionnaires and computer games and to undergo neuroimaging within a single laboratory visit. All processing and analysis scripts are freely available at https://github.com/catcamacho/socialfrustration.

2.2. Participants

The study included 58 four-to-seven-year-old children. Inclusion criteria were being safe to undergo fMRI neuroimaging (data not reported here), physically healthy and typically developing, and able to follow directions and complete games in English. Exclusion criteria included formal diagnosis of a neurological, developmental, or psychiatric disorder, or having a biological parent with a diagnosis of autism spectrum disorder, bipolar disorder, or schizophrenia. Of the 58 total children, four were removed for equipment errors in fNIRS data acquisition. Of the full sample, two children did not complete the eye tracking task (one due to interference from eyeglasses and one child completed a different version of the task). Sample characteristics are summarized in Table 1.

2.3. Child temperament assessment

Child temperament was assessed using the short form of the Child Behavior Questionnaire (CBQ-SF; Putnam and Rothbart, 2006). The CBQ-SF is a parent-reported questionnaire that assesses fifteen domains of temperament. Parents were asked to rate how true or untrue a given statement was of the child's behavior over the previous six months using a seven-point Likert scale. In the original factor analysis (Rothbart et al., 2001), these fifteen domains loaded onto three broad factors: Negative Affectivity, Surgency, and Effortful Control. This was largely replicated in our sample (factor analysis results are reported in Appendix B; factor loadings are listed in Table B1). CBQ-SF score histograms for the sample are included in Fig. A1 and summarized in Table 1. As our goal was to characterize the Negative Affectivity factor, only this broad factor score was examined in further analyses. Negative Affectivity was computed based on the results of the factor analysis, following a similar procedure as in the original CBQ formulation (Putnam and Rothbart, 2006; Rothbart et al., 2001):

$$Negative\ Affectivity = \frac{AngerFru + Discomfort + Fear + Sad + (8 - FallingReact)}{5}$$

Table 1
Sample demographics and characteristics. CBQ-SF = Child Behavior Questionnaire-Short Form.

	Temperament Analysis (N = 58)	fNIRS Analysis (N = 54)	Eye Tracking Analysis (N = 56)
Demographics			
Age *Mean* ± *SD years*	5.82 ± 1.24	5.90 ± 1.24	5.82 ± 1.25
Race *Number (percent)*			
Asian/Asian-American	1 (1.7 %)	1(1.9 %)	1 (1.8 %)
Black/African-American	8 (13.8 %)	8 (14.8 %)	7 (12.5 %)
White/European-American	42 (72.4 %)	39 (72.2 %)	41 (73.2 %)
Bi-/Multi-Racial	7 (12.1 %)	6 (11.1 %)	7 (12.5 %)
Ethnicity *Number (percent)*			
Hispanic or Latinx	6 (10.3 %)	5 (9.3 %)	5 (8.9 %)
Not Hispanic or Latinx	52 (89.7 %)	49 (90.7 %)	51 (91.1 %)
Sex *N male (percent)*	27 (46.6 %)	25 (46.3 %)	27 (48.2 %)
Annual household income *Mean* ± *SD thousands of dollars*	120 ± 99	121 ± 103	120 ± 101
CBQ-SF Temperament *(Mean ± SD)*			
Negative Affectivity			
Anger/Frustration	4.29 ± 1.06	4.27 ± 1.09	4.25 ± 1.05
Sadness	4.29 ± 0.77	4.31 ± 0.77	4.26 ± 0.73
Fear	3.76 ± 1.08	3.71 ± 1.10	3.79 ± 1.07
Discomfort	4.27 ± 1.20	4.25 ± 1.23	4.21 ± 1.16
Falling Reactivity	4.74 ± 1.12	4.80 ± 1.11	4.74 ± 1.09
Surgency			
Activity	4.69 ± 0.92	4.72 ± 0.92	4.72 ± 0.91
Approach	5.08 ± 0.84	5.09 ± 0.83	5.07 ± 0.83
High Intensity Pleasure	4.79 ± 1.11	4.83 ± 1.11	4.82 ± 1.11
Impulsivity	4.22 ± 1.07	4.30 ± 1.02	4.25 ± 1.07
Shyness	3.46 ± 1.20	3.40 ± 1.20	3.41 ± 1.19
Effortful Control			
Inhibitory Control	4.98 ± 0.91	4.92 ± 0.91	4.95 ± 0.90
Perceptual Sensitivity	5.23 ± 0.85	5.21 ± 0.87	5.23 ± 0.86
Attention Focusing	5.05 ± 0.89	5.00 ± 0.90	5.02 ± 0.89
Low Intensity Pleasure	5.82 ± 0.75	5.79 ± 0.76	5.80 ± 0.75
Smiling/Laughter	5.97 ± 0.74	6.02 ± 0.70	5.98 ± 0.71
Cake Game Affect Ratings *(Condition-Feedback Mean ± SD)*			
Social-Positive	–	1.74 ± 1.35	–
Social-Negative	–	1.22 ± 1.69	–
Nonsocial-Positive	–	1.97 ± 1.18	–
Nonsocial-Negative	–	1.10 ± 1.54	–
Picture Viewing Task Fixations *(Number of fixations Mean ± SD)*			
Happy Faces			
Eyes	–	–	1.28 ± 0.79
Mouths	–	–	1.48 ± 0.98
Angry Faces			
Eyes	–	–	1.02 ± 0.70
Mouths	–	–	1.18 ± 0.82

Though not the focus of this analysis, Effortful Control has also been associated with emotion regulation development (Eisenberg et al., 2011), thus we have included this analysis in Appendix C.

2.4. Frustration task

Children completed a modified version of the Incredible Cake Kids (Grabell et al., 2019; Murty et al., 2020) game modified to include social and nonsocial contexts presented in a block design during functional Near-Infrared Spectroscopy (fNIRS) imaging. Briefly, children were instructed to bake cakes before the bakery opened (Nonsocial blocks) to sell to customers once the bakery is opened (Social blocks). Nonsocial blocks included trials in which children selected cakes to be baked in an oven. In Positive feedback trials, the oven successfully produced an attractive cake accompanied by verbal feedback (e.g., "All done"). In Negative feedback trials, the oven would instead produce a burnt cake accompanied by verbal feedback (e.g., "Bake fail"). Social blocks included trials in which children selected a personalized cake for a customer who entered the bakery. In Positive feedback trials, the customer loved the cake and smiled at the child with verbal feedback (e.g., "Yummy!"). In Negative trials, the customer disliked the cake, displaying a frown and angry eyebrows with verbal feedback (e.g., "Gross!"). Nonsocial and Social blocks were interleaved to maintain narrative structure in the game while the block feedback condition (Positive versus Negative) was randomized. After each block, children were asked to rate how they currently felt on a 7-point scale from a deeply frowning face (-3) to a very happy face (3). Each condition-feedback combination was included four times, resulting in 16 total blocks. Each block presented five trials of the block condition plus one trial of the opposite feedback condition in random order to keep the game sufficiently unpredictable. Children played a practice round to ensure they understood how to play the game and use the affective rating system. An example trial of each block condition and feedback type is included in Fig. 1. Previous work from our lab has shown this feedback strategy to be an effective means of eliciting frustration in young children (Grabell et al., 2019, 2018; Perlman et al., 2015, 2014). Consistent with past work, we examined frustration activation by subtracting activation during the negative feedback blocks from the positive feedback blocks within each block condition (i.e., Social-Negative minus Social-Positive and Nonsocial-Negative minus Nonsocial-Positive).

2.5. fNIRS acquisition

As children played the modified Incredible Cake Kids game, cortical hemodynamics were imaged using a continuous-wave NIRx NIRScout system outfitted with eight sources and four detectors arranged to capture blood flow in the prefrontal cortex. Sources were placed at FC5, F5, AF3, Fp1, Fp2, AF4, F6, FC5, and detectors were placed at F7, AF7, AF8, and F8 on the 10–20 system, resulting in ten channels for analysis. Source LEDs emitted 760 and 850 nm—light wavelengths sensitive to deoxygenated and oxygenated hemoglobin (HbO)—which were measured by the detector photodiodes at sampling rate of 15.625 Hz. Source and detector optodes were placed flush against the child's scalp by fixing the optodes to an elastic neoprene cap—outfitted with plastic spacers to maintain a 3 cm distance between optodes—that was then fitted to the child's head by measuring the child's head circumference and selecting a cap of that size. Caps were placed in a standardized fashion over the head, with the front of the cap aligning just above the eyebrows. Caps were snug enough to not move during typical acquisition conditions. Before acquisition, the signal gains were calibrated to the child and optode placement was adjusted by parting hair or applying spring-loaded grommets as needed to optimize signal quality. Channels that failed to calibrate effectively or lost contact during acquisition were noted and excluded from analysis. During acquisition, if the cap moved away from the standardized location, it was immediately adjusted. Channels and optode arrangement are depicted in Fig. 2.

2.6. fNIRS processing and analysis

All fNIRS processing and analysis was carried out using the NIRS Brain AnalyzIR toolbox (Santosa et al., 2018) in MATLAB 2019b (The MathWorks, Inc., Natick, Massachusetts, USA). Signals were first converted to optical density using the modified Beer-Lambert equation, then Temporal Derivative Distribution Repair was applied to correct for motion artifacts (Fishburn et al., 2019) before resampling the signal to 5 Hz. Only HbO signals were examined in further analyses. Channels were visually inspected for signal quality—those that had failed to calibrate during acquisition (i.e., signal dominated by high frequency noise with little low frequency fluctuation) were removed from further analysis. Overwhelmingly, the removed channels were the posterior-most channels (one and ten). There was no correlation between the number of channels dropped and age (Mean channels retained = 8.6; range = 6–10; Spearman's $r=-0.01$, $p = 0.964$). The box car function for each block

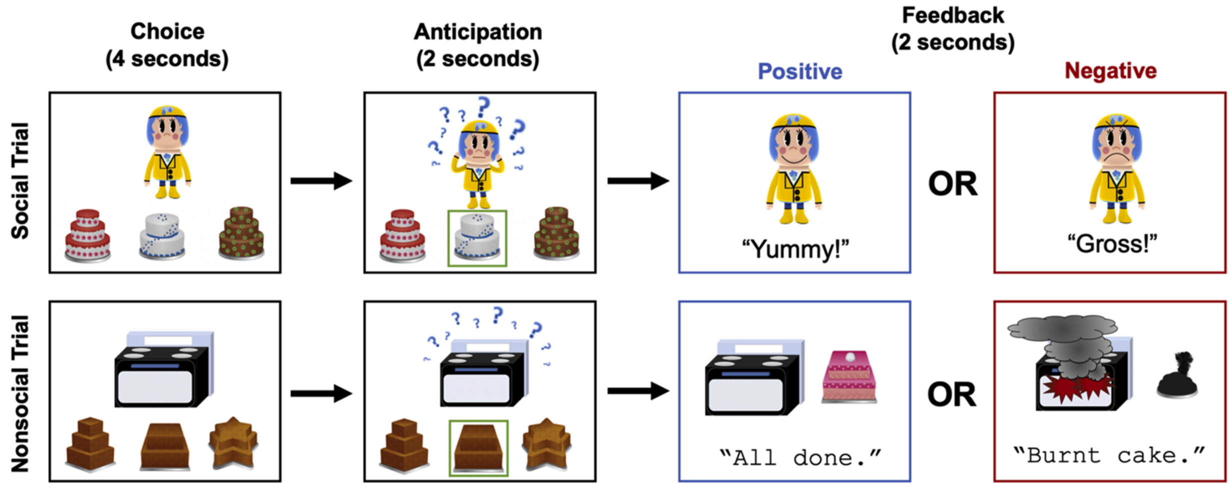

Fig. 1. Modified Incredible Cake Kids task schematic. Children played a modified version of the Incredible Cake Kids game during fNIRS imaging. Blocks included six trials, five of the block feedback type and one trial of the opposite feedback. Nonsocial blocks always preceded Social blocks to maintain narrative consistency while the Feedback condition was randomized. The game included a total of 16 blocks, 4 blocks of each Condition-Feedback type (Social-Positive, Social-Negative, Nonsocial-Positive, Nonsocial-Negative).

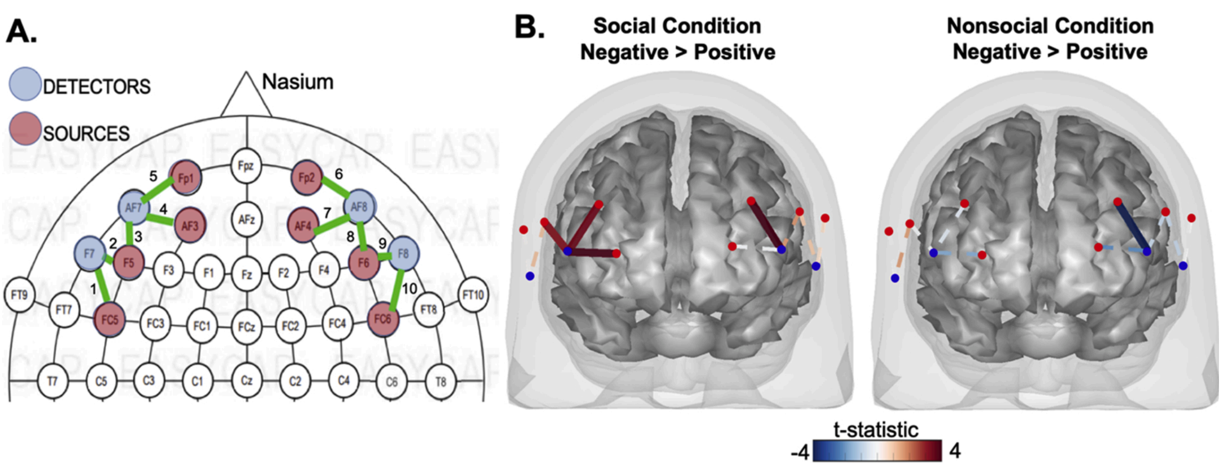

Fig. 2. Group Level Prefrontal Activation During Social and Nonsocial Frustration. A. schematic of the source and detector optode placement visualized and labeled according to the 10-20 system. Plastic spacers ensured a standard distance of 3 cm between detectors and sources. **B.** Channels with significant activation after controlling for the false discovery rate ($q<0.05$) are visualized in solid lines and non-significant channels are shown as dashed lines. The expected "frustration effect"—increased prefrontal activation in the Negative feedback compared to Positive feedback—was found in the Social condition only.

convolved with the canonical 6-second-peak hemodynamic response function (HRF) was modeled as a separate regressor in a general linear model (GLM) to compute subject level activation for each channel. Temporal and dispersion derivatives were also included in the GLM and discarded to account for individual variability in the HRF.

To identify significant group-level activation patterns, a mixed effects ANOVA was conducted with subject entered as a random effect and condition-feedback (Social/Nonsocial, Positive/Negative) as a fixed effect. Two one sample t-tests were conducted on the resulting t-statistics (Social-Negative minus Social-Positive and Nonsocial-Negative minus Nonsocial-Positive), controlling for multiple comparisons across ten channels (Benjamini and Hochberg, 1995). Channel activation was considered significant at a false discovery rate (FDR) corrected $p < 0.05$, or $q<0.05$. Significant channel activation was then combined into a single region of interest (ROI) before parameter estimates (betas) were extracted for further analysis.

2.7. Viewing affective faces

In order to capture attentional patterns, children completed a free-viewing picture task modified from a previous version (Perlman et al., 2009) and administered via the native SMI Experiment Center (Teltow, Germany) software. Briefly, children were seated at a table with a laptop placed in front of them, facing a blank wall to limit distractions from the screen. Children were then instructed to look at pictures as they appeared. Pictures were either full screen, large images of affective faces (Face images) or of a collection of objects with a single affective face placed in a random location of the grid (Jumble images). Affective faces were one of 5 conditions: Angry, Fearful, Happy, Sad, or Neutral. Five images of each type and affective condition were included for a total of 50 images displayed for five seconds in a randomized order, with a three-second fixation in between. A schematic of the task is presented in Fig. A2. The task was split into two runs, each less than three minutes long in order to reduce fatigue. An experimenter sat next to the child during the task to direct the child back to the screen as needed, but did not otherwise prompt the child or remark upon the images. All affective faces were selected from the NimStim stimuli set (Tottenham et al., 2009). Here, we focus on the Angry and Happy Face images to probe what attentional patterns may be associated with Negative Affectivity in children and to relate these data to the frustration game, which features

Happy and Angry faces during feedback in the Social blocks.

2.8. Eye tracking acquisition and processing

Gaze was tracked using an SMI Remote Eyetracking System (Teltow, Germany). Specifically, infrared light was used to track the child's pupils during the Picture Viewing Task using the SMI iViewRed software. Before the start of the task, the child was placed in a booster seat in front of the system laptop at approximately 15 in. from the 17-inch screen (60 Hz refresh rate). The infrared sensor was calibrated to the child's eyes and the tracking performance was validated right before the start of each run of the Picture Viewing Task. A 5-point calibration included instructing the child to fixate on a 1 mm diameter dot, which changed locations four times during the calibration process. After this calibration run, a validation screen would appear showing the dot at each location with a 3 mm diameter circle around this dot. If the validation showed poor performance as indicated by pupil tracking outside of the circle, the calibration was repeated until satisfactory calibration performance was achieved. For one child, eye tracking failed to calibrate due to eyeglasses, and their data were excluded from analysis. The experimenter sat next to the child and angled their face away from the screen and out of view of the sensor to not contaminate the eye tracking.

Data were processed using SMI BeGaze analysis software v3.7 (Teltow, Germany). Areas of Interest (AOIs) were manually drawn on the full-screen Angry and Happy faces to delineate the eyes, mouth, and entire face. For each trial, the total fixation duration (FD) within each AOI was computed as time spent gazing within the borders of the AOI across the entire trial. The FD for each trial was then averaged across trials for each participant, resulting in one metric for each eyes, mouth, and face for each condition. Each child contributed at least one trial for each condition for analysis (Happy: Mean $\pm$ SD $= 4.6 \pm 0.8$ trials; Angry: Mean $\pm$ SD $= 4.5 \pm 1.0$ trials). There was a positive association between number of usable trials and age for the Angry condition only (Angry: Spearman's $r = 0.31$, $p = 0.020$; Happy: Spearman's $r = 0.18$, $p = 0.174$). In order to characterize specific gaze patterns, our analysis was focused on the eye and mouth AOIs as these provide insight into how children are processing the Happy and Angry faces. First, a bias score was created by subtracting mouth FD values from eyes FD values. These bias terms for each Angry and Happy faces were next correlated with Negative Affectivity. To determine what was driving resulting associations, the original four FD values were also correlated with Negative Affectivity. If only one set of FD values was correlated (e.g., mouth FD), then that was considered the main driver of the bias score association. The main driver of the association (raw FD or FD bias scores) was included in the full analysis.

2.9. Full analysis

Spearman correlational analysis was carried out using the SciPy (Virtanen et al., 2020) package in Python v3.6 (Python Software Foundation, www.python.org) to characterize associations between variables of interest: 1) Temperamental Negative Affectivity, 2) emotion regulation to frustration (Negative minus Positive feedback betas), 3) fixation duration on each eyes and mouths AOI for each Happy and Angry faces. Significant correlations between Negative Affectivity and the bio-behavioral metrics were entered into the below models to fully characterize those associations.

2.9.1. Negative affectivity and frustration activation

We used Mixed Effects Linear Modeling (MELM) carried out using the lme4 library (Bates et al., 2015) in R v3.3 (R Core Team, 2017) to test if Negative Affectivity (NegAff) was associated with frustration activation and if that association differed by child age. Specifically, the following models were conducted with Sex entered as a random intercept of non-interest:

1 $\text{Frustration}_i \sim \text{Sex (intercept)}_i + \text{NegAff}_i + \text{Age}_i$
2 $\text{Frustration}_i \sim \text{Sex (intercept)}_i + \text{NegAff}_i + \text{Age}_i + \text{Age*NegAff}_i$

Where i indicates each observation (i.e., subject). A random intercept in this context indicates that each sex will be modeled as a separate model (i.e., can have different intercepts). For more information about MELM, please see Galecki and Burzykowski, (2012). Model fit between models 1 and 2 were then compared using the anova function from the lmerTest library (Kuznetsova et al., 2016).

2.9.2. Negative affectivity and attentional patterns

Just as with the previous analysis, we used MELMs to test if Negative Affectivity was associated with attentional patterns of processing Happy and Angry faces:

1 $\text{FixationDuration}_i \sim \text{Sex (intercept)}_i + \text{NegAff}_i + \text{Age}_i$
2 $\text{FixationDuration}_i \sim \text{Sex (intercept)}_i + \text{NegAff}_i + \text{Age}_i + \text{Age*NegAff}_i$

Just as with the activation analysis, the fits of each model were compared and the model with the better fit was interpreted.

3. Results

Spearman correlations between variables analyzed here are included in Table 2.

3.1. Frustration activation

Replicating previous work examining regulation during frustration, children reported significantly less positive (more negative) affect after Negative feedback blocks than after Positive feedback blocks of the Cake Game (overall: $t(55) = 4.05$, $p < 0.001$, Cohen's D=0.57; Social: $t(55) = 2.61$, $p = 0.012$, Cohen's D=0.37; Nonsocial: $t(55) = 4.29$, $p < 0.001$, Cohen's D=0.69). Condition-Feedback affect rating means and standard deviation values are reported in Table 1. Group level results revealed the expected frustration effect in the social condition only (Fig. 2). Specifically, four channels—three on the right PFC and one on the left PFC—indicated significantly more activation in the Negative feedback condition than the Positive feedback condition during Social blocks (q<0.05). In the Nonsocial condition, only one channel significantly differed in activation between feedback conditions with less activation

Table 2
Spearman correlations between variables of interest. Significant correlations are denoted as follows: *p < 0.05, **p < 0.01, ***p < 0.005.

	2	3	4	5	6	7
1. CBQ-SF Negative Affectivity	−0.11	−0.37**	0.13	−0.27*	−0.05	−0.47***
2. Age		−0.06	0.39**	0.36**	0.09	0.30*
3. Frustration Activation (Social Condition)			−0.02	0.02	0.28*	0.13
4. Eye dwell time (Angry Faces)				0.34*	0.62***	0.46***
5. Mouth dwell time (Angry Faces)					0.28*	0.79***
6. Eye dwell time (Happy Faces)						0.37**
7. Mouth dwell time (Happy faces)						

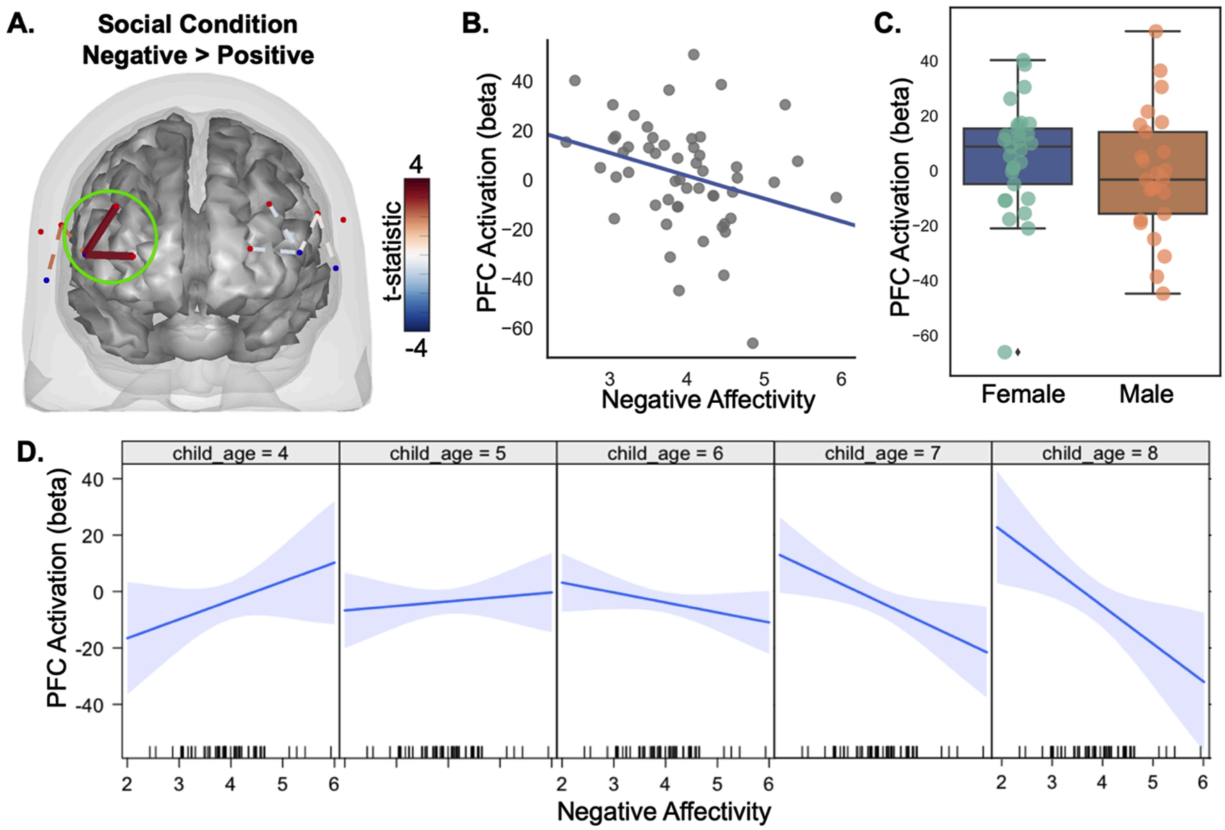

Fig. 3. Right PFC frustration activation is predicted by Negative Affectivity and moderated by age. Models 1 and 2 provided comparable fits to the data with Model 2 offering a slightly better fit (comparison $X^2 = 4.54$, p = 0.033) **A.** A region of interest (ROI; circled in green) was made to encompass the significant channels from the channel-wise group analysis. Frustration activation parameter estimates (Negative minus Positive betas) for each child were then extracted for Mixed Effects Linear Modeling. **B.** In model 1, PFC ROI frustration activation was negatively associated with Temperamental Negative affectivity (t(54)= −2.38, p = 0.021) **C.** In model 1, mean PFC ROI activation differed by Sex (model intercept; t(54) = 2.36, p = 0.022). **D.** In model 2, the Age, Negative Affectivity, and Sex terms were all non-significant (ps>0.05) with the addition of the Age*Negative Affectivity term, indicating the association between PFC frustration was moderated by age (Age*Negative Affectivity term t(54)= −2.18, p = 0.034) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

in Negative than Positive. To reduce these data for further analysis, we created four ROIs, excluding channels one and ten as one or both of these channels were missing from 38 children. The four ROIs (left and right anterior and dorsolateral LPFC) were re-analyzed, and only the ROI created from the anterior two channels remained significant after FDR correction (Fig. 3A). Thus, beta values from this ROI were extracted. All children provided data for both channels included in this ROI with the exception of two children who had data for one channel each. Frustration activation for the Social condition (Social-Negative beta minus Social-Positive beta) was significantly correlated with Negative Affectivity (r=−0.37, p = 0.006). We found trending associations between each Frustration activation and Negative feedback activation and mean mood ratings during the Social-Negative blocks (Frustration: Spearman's r(54) = 0.24, p = 0.080; Negative: Spearman's r(54)=−0.25, p = 0.074). No associations were found with regards to Positive feedback condition mood ratings.

3.2. Attentional patterns toward angry and happy faces

Fixation duration (FD) values ranged from 0 to 1709.83 milliseconds in length (Happy eyes: 529 ± 411 ms; Happy mouth: 584 ± 472 ms; Angry eyes: 388 ± 343 ms; Angry mouth: 474 ± 414). FD bias scores for both Happy faces and Angry faces were correlated with Negative Affectivity (Happy: r = 0.39, p = 0.003; Angry: r = 0.33, p = 0.003), indicating that children higher in Negative Affectivity spent more time looking at the eyes or away from the mouths of these faces. FD for the mouth regions of both Happy and Angry faces were significantly correlated with Negative Affectivity (Happy: r=−0.47, p < 0.001; Angry: r=−0.27, p = 0.046) such that higher negative affectivity predicted short FDs on the mouths of these faces. FD on the eyes of Happy and Angry faces were not significantly associated with Negative Affectivity (rs<0.13, ps>0.358), suggesting that the associations with the bias scores were driven by gaze at the mouths of these faces. Thus, only the Happy and Angry face mouth FD values were investigated in the mixed-effects models. A group-level heatmap of a representative Happy face image is included in Fig. 4A and a heatmap of gaze towards a representative Angry face is included in Fig. A4A.

3.3. Full analysis: frustration response and negative affectivity

Social Model 1: The Sex intercept term and Negative Affectivity terms each significantly predicted PFC frustration activation such that children higher in Negative Activity demonstrated lower activation (t(54)=−2.38, p = 0.021; Fig. 3B) and female children had higher activation on average (t(54) = 2.36, p = 0.022; Fig. 3C). The Age term was not significant (t(54)=−0.81, p = 0.422). Social Model 2: The Age*Negative Affectivity term in the second model significantly predicted PFC frustration activation such that there was the negative association between PFC activation and Negative Affectivity was strongest in the oldest children (t(54)=−2.18, p = 0.034; Fig. 3D). Other model terms were in the same direction as in Model 1 though less strongly when contextualized with the interaction term (Age t(54) = 2.00, p = 0.050; Negative Affectivity t(54) = 1.66, p = 0.102; Sex t(54)=−1.46, p = 0.151). Social Model Comparison: Model 2—which included the

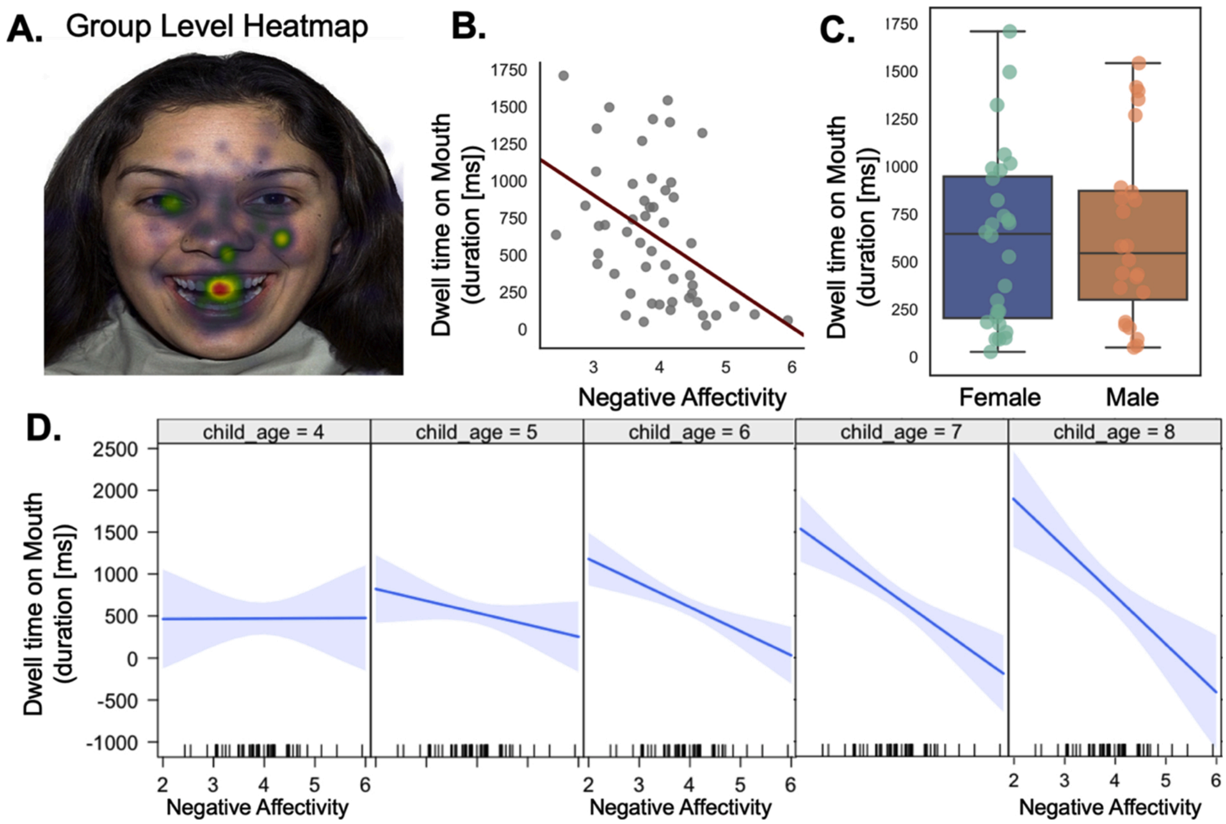

Fig. 4. Dwell time on the mouths of Happy faces is predicted by Negative Affectivity and moderated by Age. Models 1 and 2 provided comparable fits to the data with Model 2 offering a slightly better fit (comparison X^2=4.27, p=0.039) **A.** Group level summary of gaze behavior for a representative Happy face. Warmer colors indicate longer time spent gazing at that region on average. **B.** In model 1, increased Negative Affectivity predicted significantly shorter dwell time on the mouth of Happy faces (t(52)=−3.76, p<0.001). **C.** In model 1, mean mouth dwell time differed by Sex (t(56)=2.83, p=0.006). **D.** In model 2, the Negative Affectivity and Sex terms were non-significant (ps>0.201) with the addition of the Age*Negative Affectivity term in the model (t(56)=−2.11, p=0.040).

Age*Negative Affectivity interaction term—provided a slightly better fit to the data than Model 1 (Model 1 AIC = 488.3, BIC = 498.3; Model 2 AIC = 485.8, BIC = 497.7; comparison X^2 = 4.54, p = 0.03).

While there were no activation outliers across the sample, one outlier for females can be observed in the activation plots by sex. To ensure that modeling the sex term was not driving the observed associations between age, negative affectivity, and activation, we conducted a follow-up multiple linear regression of the same formula as the mixed-effects models minus the sex intercept term. The results were nearly identical, including that Model 2 provided a better fit to the data with a significant Age*Negative Affectivity term. Further, to contextualize these findings, we have reported the results modeling nonsocial activation in Appendix E.

3.4. Full analysis: attentional patterns and negative affectivity

Angry Model 1: The Age term significantly predicted how much time children spent gazing at the mouth of Angry faces such that older children spent more time gazing at the mouth (t(56) = 2.61, p = 0.012). The Negative Affectivity term was only marginally significant indicating that children higher in Negative Activity generally looked at the mouth for less time (t(56)=-1.74, p = 0.087; Fig. A4B). The Sex intercept term was not significant (t(56) = 1.00, p = 0.320). Angry Model 2: None of the model terms significantly predicted gaze behavior (ts<1.52, ps>0.134). Model Comparison: Model 2 did not provide a better fit to the data than Model 1 (Model 1 AIC = 833.7, BIC = 843.7; Model 2 AIC = 834.5, BIC = 846.7; comparison X^2 = 1.17, p = 0.279).

Happy Model 1: All terms were significant in predicting fixation duration (FD) on the mouths of Happy faces, such that older children had longer FD and children higher in negative affectivity had shorter FD (Negative Affectivity: t(56)=−3.76, p < 0.001; Age: t(56) = 2.27, p = 0.027; Sex intercept: t(56) = 2.83, p = 0.006; Fig. 4B–C). Happy Model 2: The Age*Negative Affectivity term was a significant predictor of Happy face mouth FD such that the negative association between FD and Negative Affectivity was primarily found in older children (t(56)=−2.11, p = 0.040; Fig. 4D). The Age term was also positively associated with Happy face mouth FD (t(56) = 2.48, p = 0.016) while the Negative Affectivity and Sex intercept terms were not significant (Negative Affectivity: t(56) = 1.30, p = 0.201; Sex intercept: t(56)=-1.24, p = 0.222). Model Comparison: Model 2 provided a slightly better fit to the data (Model 1 AIC = 841.6, BIC = 851.7; Model 2 AIC = 839.3, BIC = 851.5; comparison X^2 = 4.27, p = 0.039).

Since an association was found between age and usable trials, analyses were repeated with the number of usable trials included as a covariate (Appendix F). Results were largely the same. For completeness of reporting, we have also included an analysis of the full face AOIs (Appendix G), an analysis of the first fixation times and fixation latency (Appendix H), and repeated the analyses with Fear, Sad, and Neutral faces (Appendix I).

4. Discussion

In this study, we sought to index multi-modal affective processing systems associated with temperamental Negative Affectivity and characterize the associations between these systems and age in early childhood. Similar to past work on emotion regulation(Belden et al., 2015; Goldin et al., 2008; Grecucci et al., 2013; Ochsner and Gross, 2005), we found bilateral prefrontal cortex (PFC) activation in response to social frustration, with activation in more channels in the right lateral PFC. We found age-dependent associations between these systems and Negative

Affectivity. Specifically, right anterior-lateral PFC activation during socially-cued frustration was negatively associated with Negative Affectivity primarily in older children. Total fixation duration on the mouth portion of Happy faces was also negatively associated with Negative Affectivity primarily in older children. The age-dependence of our findings suggest an emerging coordination of these bio-behavioral systems across early childhood. Considering the intense development across this age, a full characterization of the biological systems that underlie Negative Affectivity could provide important information for understanding precursors to psychopathology.

We found evidence that children high in Negative Affectivity attended to the mouths of Happy faces less and engaged less prefrontal regulation during socially-cued frustration, effects that were driven by the older children. These associations potentially point to differences in automatic attention to positive socio-emotional cues as well as differences in top-down regulation which could ultimately contribute to increased or prolonged experiences of negative affect in these children across development. This combined tendency could indicate that children high in Negative Affectivity may be less likely to reinforce positive social feedback, internalizing more negative environmental learning than positive, which may explain the oft observed negative biases in older youth high in internalizing symptoms (Salum et al., 2017). That we found effects primarily in older children supports this theory, since older children will have had more time to shape their affective systems in response to environmental cues. Interestingly, we did not observe this same age by Negative Affectivity interaction in our models examining attention allocation to the entire Happy face. As mentioned in the introduction, very little work has been done to examine how children high in Negative Affectivity process specific facial features and instead most work has examined biases for attending to entire faces. Thus, it is possible that future work examining attention to specific facial features could provide further nuance to our understanding of attentional biases in disorders associated with Negative Affectivity as well as provide further insight into naturalistic social processing. Mapping the changes in attention allocation to specific facial features—particularly of those features rich in emotional information such as the mouth and eyes—across development and across children with high Negative Affectivity could provide important insight into the role of attentional biases in the etiology and course of mood and anxiety disorders.

We also found evidence for the potential coordinated development of the biobehavioral systems that give rise to emotion processing and regulation across early childhood related to Negative Affectivity. Behavioral research has found that children undergo dramatic improvements in being able to correctly identify basic emotional faces and states across the early childhood period, with more rapid development in identifying positive versus negative content (Boyatzis et al., 1993; Camras and Allison, 1985; Chronaki et al., 2015; Durand et al., 2007; Gao and Maurer, 2010). Concurrent to this development is improvements in executive functioning and emotion regulation (Hendry et al., 2016; Rothbart et al., 2011, 2007), individual differences of which are associated with temperamental Effortful Control, a broad factor that negatively covaries with Negative Affectivity (Putnam et al., 2014; Rothbart et al., 2001). In adolescent and adult work, there is extensive evidence for lateral and medial PFC engagement during deliberate reappraisal of emotional content (Buhle et al., 2014; Ochsner et al., 2012; Silvers et al., 2017) and some evidence that enhancement of PFC activation and reduction of amygdala activation during emotion regulation is associated with improved emotion regulation (Nicholson et al., 2017), suggesting that maturation of the bidirectional PFC and limbic circuitry connections is likely involved in early emotional learning and shapes long-term emotional tendencies. Indeed, in rodent work, there is evidence that limbic and PFC activity changes in response to learning and that these changes are critical for altering future emotional responses to a given stimulus (Milad et al., 2006; Rosas-Vidal et al., 2018; Sotres-Bayon and Quirk, 2010). There is also evidence to suggest that the adult limbic circuitry differentiates adults with high childhood behavioral inhibition and increased co-occurring internalizing symptoms from those without high internalizing symptomology (Hardee et al., 2013). Thus, it is highly likely that improvements in identifying emotional information interact with improvements in emotional regulation via reciprocal neural connections which are dramatically shaped across early childhood. Future work must parse how changes in this circuitry shift with improvements in emotion identification and regulation abilities as well as what other system behaviors (e.g., gaze) further predict these longitudinal changes.

We also found evidence for frustration effects in social but not non-social contexts. These findings lend support to the notion that affective neurodevelopmental work—particularly in children—benefit from more naturalistic and complex approaches which include the social context for affective information. Given that children in early childhood are still developing their abilities to identify emotions (Boyatzis et al., 1993; Chronaki et al., 2015; Durand et al., 2007), they likely rely more heavily on social cues to contextualize emotional content than adults. This rationale is in line with the long-studied social information processing theory (Crick and Dodge, 1994; Lemerise and Arsenio, 2000). More recent work has demonstrated that children show strong neural activation to stimuli presented within a more complex, naturalistic context (Camacho et al., 2019; Cantlon and Li, 2013; Karim and Perlman, 2017; Richardson et al., 2018). Thus, further work mapping neurodevelopment of socio-emotional cognition systems would benefit from using complex emotional stimuli for studying early childhood, an age at which children have a difficult time tolerating repetitive fMRI tasks (Camacho et al., 2020).

This study has several notable strengths. First, we used engaging games and multimodal approaches tailored to young children to assess systems that govern all stages of emotion processing in the same sample. Second, we used a data-driven approach to characterize these systems—and Negative Affectivity—in our sample of children. Third, we used a model fitting procedure to examine how these systems are associated with Negative Affectivity across age. Finally, we examined how children process emotional faces by examining the specific facial regions they fixated upon. There are also several important limitations to this work that should be carefully considered for future studies examining these systems. First, this study is cross-sectional, thus the associations we found across age must be replicated in a longitudinal study. Second, fNIRS imaging—while excellent for maintaining compliance and a more naturalistic assessment environment for young children (Gervain et al., 2011)—is limited to recordings from the surface of the cortex. In this study, we only measured the PFC, thus are not able to directly analyze the coordination between the PFC and brain systems that integrate information. Furthermore, since we were unable to co-register the fNIRS data to head models of each subject, the anatomical boundaries of the ROIs tested here are not as precise as with other neuroimaging and registration methods, which limits our understanding of the anatomical specificity of these results. Future work using a whole-brain method could provide further important insight to these systems. Third, the sample size is relatively limited in power to detect small effects, which many affective processes may prove to be. Future work must aim to replicate these findings in larger samples. Lastly, while our paradigms were naturalistic in many ways, they do not communicate the full, complex, and dynamic process through which children experience affective information. Further work using dynamic and complete stimuli could therefore provide a more nuanced insight to how these bio-behavioral systems associated with Negative Affectivity change across early development.

5. Conclusions

While our sample was not selected for psychopathology, these findings have implications for early risk assessment for emotion dysregulation disorders. High temperamental Negative Affectivity in early childhood is predictive of later psychopathology. The present study serves as one more step in fully characterizing the neurobiological development of the systems that comprise Negative Affectivity—further work characterizing the development of these systems across early childhood will provide invaluable insight to not just which children are likely to develop psychopathology, but also how we may intervene to support these children. Importantly, this work provides the first step toward multi-modal assessment of early childhood Negative Affectivity systems, with evidence that integration of bio-behavioral systems occurs across early childhood. Further work is needed to fully elucidate these developmental trajectories through longitudinal and multi-modal assessment of early childhood emotional development.

Data statement

Data and task paradigms are available upon reasonable request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.dcn.2021.100917.

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